MEDICINE SURGERY OBSTETRICS GYNAECOLOGY

CUMULATIVE SUPPLEMENT
1939

MEDICINE SURGERY OBSTETRICS GYNAECOLOGY

Under the General Editorship of

SIR HUMPHRY ROLLESTON, BT.
G.C.V.O., K.C.B., M.D., D.Sc., D.C.L., LL.D.
EMERITUS REGIUS PROFESSOR OF PHYSIC, CAMBRIDGE
SOMETIME PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS OF LONDON

Publishing Editor
ADAM CLARK, L.M.S.S.A.

Sub-Editor
G. FAULKNER, D.Sc.

CUMULATIVE SUPPLEMENT
1939

AFFILIATED EAST-WEST PRESS PVT. LTD.
NEW DELHI

AFFILIATED EAST-WEST PRESS PVT LTD

Published January 1940

Published by W. D. Ten Broeck for AFFILIATED EAST-WEST PRESS PRIVATE LTD., C 57 Defence Colony New Delhi 3, India, and printed by S. M. Balsaver at USHA PRINTERS, National House, Tulloch Road, Bombay 1, India.

PUBLISHERS' ANNOUNCEMENT

In order to keep the BRITISH ENCYCLOPAEDIA OF MEDICAL PRACTICE up to date, an annual Supplemental Service is being published. This will be comprised in two annual volumes; one will be cumulative, and the other will consist of surveys and abstracts.

CUMULATIVE SUPPLEMENT

The purpose of this volume is to present new medical information which has become available since the publication of the original work, and which has already been accepted as likely to form an established part of medical knowledge. In this, the first Annual Cumulative Volume, the material has in many cases been supplied by the authors of the original articles in the Encyclopaedia, though the final responsibility for its inclusion must rest with the Editors.

The material in this volume should be read in conjunction with the original volumes of the Encyclopaedia, since in effect it forms a continuation of the latter. Ease of reference between the two is ensured by the series of key numbers which will be found at the top of each right-hand page of the original volumes. By referring to the corresponding key number in this Cumulative Volume, the reader will at once find any new information which has become available on a particular subject.

This volume will be replaced annually by a new volume, which will be cumulative, i.e. it will incorporate all relevant matter in the previous volume or volumes, together with the latest information. Thus it will be necessary, in order to be up to date, to turn to one volume and one volume only, viz. the latest Annual Cumulative Volume. If this plan is well received by subscribers, the Publishers hope to keep it in being for at least seven years.

SURVEYS AND ABSTRACTS

The explanation of the plan and scope of this volume will be found in the foreword thereto.

BUTTERWORTH & CO. (PUBLISHERS), LTD.

CUMULATIVE SUPPLEMENT 1939

ABDOMINAL PAIN AND ACUTE ABDOMINAL EMERGENCIES

See also Surveys and Abstracts 1939, p. 181

DIAGNOSTIC SIGNIFICANCE OF PAIN

A series of investigations on the distribution of pain radiated from points of stimulation of the deeper somatic sensory nerves is recorded by Kellgren, who stimulated the interspinous ligaments and other deep structures such as bone and periosteum, in human subjects, using as a stimulus the hypodermic injection of 0·1 to 0·3 c.cm. of 6 per cent saline solution. The pain produced in the interspinous ligaments, when at its maximum, showed a segmental distribution associated with deep tenderness in the same area. It was impossible to classify the pain produced into 'local' and 'referred', since there was a gradual transition from pain confined to the region stimulated to diffuse pain of full segmental distribution. Instead Kellgren describes (i) pain which is moderately well localized, obtained from the more superficial body coverings, and (ii) diffuse pain of segmental distribution obtained from the more deeply situated structures. He considers that the segmental distribution of diffuse pain may be a form of false localization.

This paper is an important preliminary to another by Lewis and Kellgren, who first extended Kellgren's earlier observations on stimulation of the interspinous ligaments in man to determine the extent of the associated muscular rigidity and cutaneous hyperalgesia. On stimulation of the 1st lumbar ligament they observed, in addition to pain with the distribution of renal colic, retraction of the testis. Cutaneous hyperalgesia was found in 4 out of 5 subjects. From the 9th thoracic interspinous ligament they found reflex contraction of the upper belly of the corresponding rectus abdominis. Deep tenderness corresponded with the muscular rigidity, and a little later cutaneous hyperalgesia appeared, though its area was not the same as that of deep tenderness. From these experiments it was concluded that there is a common, though complex, mechanism which is stirred into activity by afferent impulses derived either from deep-lying somatic structures or from disturbance of a viscus. Further evidence in support of this view was provided by injection of the interspinous ligament below the 7th cervical or 1st thoracic spines in patients suffering from angina of effort; the pain induced, radiating down the left arm, was found by the patient to be of the same kind as the anginal pain. In the light of these experiments the authors do not believe that the pain derived from the deep somatic structures is distinct in character from that due to visceral disturbances.

Experiments on the decapitated cat were carried out to investigate the muscular reflex of somatic and visceral origin. Injection of 10 per cent saline solution into the interspinous ligament at the 12th and 13th thoracic vertebrae produced a tonic contraction of the rectus. Pinching the back muscles with forceps produced reflex contraction of the rectus of a few seconds' duration.

The abdominal organs were next examined, a pinch stimulus being used. No contraction of the rectus muscle was obtained by pinching the kidney, spleen, or liver, nor from any part of the stomach or bowel. The mesenteries of the ileum, jejunum, and colon yielded occasional reflexes, especially when the pinch included the large vessels of the mesentery. Pulling on any of these mesenteries usually gave a response. The great omentum did not give rise to any response except at its root where it contains the tail of the pancreas. The gall-bladder gave no response, but pinching in the region of the common bile-duct induced vigorous responses. The duodenal loop was found to be most satisfactory for experiment; its mesentery contains the pancreas as well as the intestinal vessels. Pinching the intestine alone never caused any response of the abdominal muscles, nor did distension of the duodenum by a balloon give rise to this muscular reflex. Pinching the mesentery, however, gave an immediate response. Lewis and Kellgren considered, for reasons that are not

1 convincing, that it is stimulation of the *pancreas* rather than of the *mesentery* that gives rise to this reflex. Since, however, the same reflex is obtained from other parts of the mesentery that do not contain any pancreas, this would seem to be an error, and to confuse the issue. The point to be kept in mind is that it is only from nerves that are sensitive to mechanical stimulation, such as pinching, that reflex contraction of the abdominal muscles arises, and that no such nerves are present in the wall of the gastro-intestinal tract itself. Section of the splanchnic nerves abolishes the reflex from the mesentery, and it has long been recognized that afferent nerves from the mesentery run in these nerves on their way to the posterior roots of the spinal nerves.

In discussing the import of their experimental findings, Lewis and Kellgren return to the view of Lennander, long discarded by most authorities in Great Britain, that there is no true visceral pain, and that all the pain of visceral disease is essentially somatic in origin, or at any rate does not differ in its physiological mechanism from pain caused by simple stimulation of the mesentery. It is true that this conclusion is a little obscured by their insistence upon the pancreas as a source of motor reflexes in the abdominal wall when stimulated mechanically but, as has been pointed out, this phenomenon would seem to depend upon the inclusion of the pancreas within the mesentery of the cat's duodenum, and it would seem to be the nerves of the mesentery rather than of the pancreas that give rise to the reflex.

The most significant finding in their experiments appears to be the complete absence of any such motor reflexes when the intestine itself is stimulated, either by pinching or by inflating a balloon within it.

J. Morley finds it difficult to accept their view that there is no true visceral pain apart from stimulation of somatic nerves in the mesentery or parietal peritoneum by abnormal peristalsis or inflammation of the gut. The condition of strangulated Richter's hernia, in which only a portion of the intestine on its anti-mesenteric border is involved, gives rise to severe spasms of colicky pain, as does the impaction of a large gall-stone in the small intestine. In neither of these conditions can it be supposed that there is any mechanical stimulation of somatic nerves in the mesentery. Further, if the view of Lewis and Kellgren were correct, there would be expected just as sure a reflex contraction of the rectus when a balloon is inflated in the duodenum as when the mesentery is pinched, whereas their experiments proved that this reflex never occurs in the balloon experiment.

Morley therefore is convinced that their work does not disprove the existence of a true visceral pain, unassociated with any deep tenderness or hyperalgesia or reflex contraction of the muscles in the abdominal wall. Their experiments moreover go to prove the hypothesis, laid down by Morley in 1931, that a viscero-motor reflex or viscero-cutaneous radiation does not occur from the gastro-intestinal tract, and that the somatic manifestations in the abdominal wall that have been regarded by many, from Mackenzie onwards, as originating from the gastro-intestinal tract are really due to stimulation of deep-seated somatic nerves in the sensitive portion of the mesentery or the parietal peritoneum. These remarks apply to the gastro-intestinal tract only, and not to the urinary or cardio-vascular systems.

Kellgren, J. H. (1939) *Clin. Sci.*, **4**, 35.
Lewis, T., and Kellgren, J. H. (1939) *Clin. Sci.*, **4**, 47.
Morley, J. (1931) *Abdominal Pain*, Edinburgh

ABORTION

See also Surveys and Abstracts 1939, pp. 30 and 182

NATURAL AND UNINTENTIONAL ABORTION

Preventive Treatment

Progesterone

12 Now that progesterone, the active principle of the corpus luteum, can be prepared synthetically and therefore more cheaply it is more readily available for use in clinical practice

The use of progesterone in the treatment of habitual abortion is based on the results of experimental research on lower animals. The presence of the corpus luteum, or the administration of active extracts of corpus luteum or of chemically pure progesterone, is necessary for the maintenance of normal pregnancy in the

rabbit. In the human subject the corpus luteum retains its activity until the fourth month of pregnancy, degenerating slowly thereafter until, by about the sixth or seventh month, there is little evidence of its presence. It has been shown that there is less than one international unit of progesterone in 40 g. of human corpus luteum, and it would appear probable that the production and utilization of the corpus luteum hormone are continuous and that there is little storage of it in the body.

A considerable amount of recent clinical work has demonstrated the definite value of progesterone therapy in certain types of unintentional abortion. The optimal dosage to be employed awaits the results of further clinical work.

C. A. Elden reported the results of progesterone therapy in 8 cases of habitual abortion, his general method of treatment consisting of the intramuscular injection of one international unit weekly as soon as pregnancy was established until the sixth lunar month of pregnancy. No other endocrine preparation was given. The total dosage of progesterone ranged from 10 to 44 international units in the individual cases. Of these 8 patients there were two failures; one was due to an operative laceration of the cervix, but the cause of the other could not be ascertained. All the other cases were brought successfully to term, and the infants were apparently normal. Four of the 8 patients had some spotting and one had spotting with cramps. Elden suggested that smaller doses of progesterone than one unit weekly may be sufficient to carry a pregnancy to term.

M. F. Potter gave large doses of corpus luteum extract (up to 18 gr. daily) by mouth, to a series of 19 patients with a history of still-births and abortions. In these there resulted 16 successful pregnancies and only 3 failures, whereas previously, without corpus luteum therapy, of a total of 55 pregnancies among the same 19 patients 47 had failed.

S. B. Peters has recently treated 4 cases of recurrent spontaneous abortion with bi-weekly intramuscular injections of preparations containing approximately one international unit of progesterone. In all these cases the blood Wassermann reactions were negative and nothing in the history, clinical examination, or laboratory investigations was found to account for the abortions. Treatment was begun immediately a diagnosis of pregnancy was made and was continued up to, and including, the fifth month of pregnancy. In all cases pregnancy continued to term and normal living infants were born. Peters suggested that progesterone is a specific for some types of recurrent abortion and premature labour.

For information concerning ethinyl testosterone, a synthetic substance with a biological action similar to that of progesterone, see Surveys and Abstracts 1939, p. 110.

CLINICAL ASPECTS OF ABORTION

Clinical Varieties

Septic Abortion

Sulphanilamide.—B. J. Hanley and D. Golenternek investigated the value of sulphanilamide in post-abortal and puerperal infections. Of 150 cases, 75 were given sulphanilamide together with other routine measures which appeared to be indicated, and the other 75 were given similar treatment without the sulphanilamide. Of the 75 patients receiving sulphanilamide, 32 showed apparent improvement, such that the average period of stay in hospital was shortened by 2·8 days as compared with the similar group which did not receive sulphanilamide; in 20 cases the results were considered to be doubtful, as minor complications occurred; and in 23 the results were of no comparative value. This last group, however, included all the cases in which the infection had extended beyond the walls of the uterus, leading to peritonitis, septicaemia, pelvic abscess and other complications. In no case of thrombophlebitis was any improvement noted.

Treatment

F. Holtz studied the results of different methods of treating abortion, in 2,718 cases, as carried out in 3 obstetrical clinics in Stockholm. He distinguished abortions occurring in the first 3 months of pregnancy, of which there were 1,583 cases, from abortions or premature births occurring in from the fourth to the seventh month. With regard to the first group Holtz states that in uncomplicated cases without severe haemorrhage both the immediate and the late results were better after active treatment consisting of prompt emptying of the uterus by means of Saenger's forceps and curettage. It was found that spread of infection occurred less often, that the mortality was lower, that the period during which the patient was confined

to bed was of shorter duration, and that subsequent sterility was less frequent than after conservative treatment. In febrile cases the better results of active treatment were particularly noticeable. In a follow-up study of patients in this group, carried out at least 4 years after the abortion, it was found that conservative treatment was followed by sterility more frequently than active treatment, and also that tubal pregnancy was more common after conservative treatment.

With regard to abortions occurring during the later months of pregnancy, in most cases both the foetus and the placenta were expelled spontaneously with or without the aid of oxytocics. The results of expectant treatment were good both in febrile and non-febrile cases. Only in cases with retention of the placenta did the need for active treatment arise, and in such cases conservative treatment gave rise to a higher morbidity and a longer period of hospitalization. A follow-up of this group 4 years or more after the abortion showed that active treatment in cases of retention of the placenta gave as good late results as conservative treatment in cases without retention of the placenta.

From this study it would appear that the treatment of cases of abortion during the first 3 months of pregnancy should be active, whereas, after the third month, treatment should be conservative, except in cases of retention of the placenta.

ARTIFICIAL AND INTENTIONAL ABORTION

Legal Position of Practitioner

The case of R v Bourne, which was tried at the Old Bailey on July 19th, 1938, is distinguishable from other abortion cases in that the bona fides of the defendant, Mr. Bourne, were never in doubt for a moment; and in that respect the case was unique as far as the law courts are concerned. Mr. Justice Macnaghten who tried the case himself said: 'The operation was performed openly in one of our great hospitals by a man of the highest skill it was performed as an act of charity, without fee or reward, by a surgeon who unquestionably believed that he was doing the right thing and that he ought, in the performance of his duty as a member of a profession devoted to the alleviation of human suffering, to do it'.

The provision under which Mr Bourne was tried is S 58 of the Offences Against the Person Act, 1861, and the material words of the section are 'Whosoever, with intent to procure the miscarriage of any woman, whether she be or be not with child, shall unlawfully administer to her or cause to be taken by her any poison or other noxious thing or shall unlawfully use any instrument or other means whatsoever with the like intent, shall be guilty of felony'.

The Bourne case turned entirely on the question as to whether the operation was performed 'for the purpose only of preserving the life of the mother', a defence which of course is not open to the professional abortionist. The expression does not appear in the 58th section of the Offences Against the Person Act, 1861, the provision under which Mr. Bourne was tried, but as a proviso to S. 1 (1) of the Infant Life (Preservation) Act, 1929, relating to 'child destruction' (i.e. causing a child to die before it has a separate existence from its mother); but the judge declared that the words were in accordance with the Common Law as to abortion, and were implied in the 58th section of Act of 1861 by the word 'unlawfully' used therein.

The case thus resolved itself into a discussion as to the meaning and implications of the words 'for the purpose only of preserving the life of the mother'. It was suggested by the prosecution that there is a distinction between danger to health and danger to life; but the judge said that in his opinion no such clear dividing line exists and he quoted a reply of Mr Bourne. 'There is a large body of material . . . in which it is not really possible to say how far life will be in danger but we find, of course, that the health is depressed to such an extent that their life is shortened, such as cardiac cases, so that you may say that their life is in danger, because death might occur within measurable distance of the time of their labour'. The words have to be construed in a reasonable sense and, if the doctor is of opinion on reasonable grounds and with adequate knowledge that the probable consequence of the continuance of the pregnancy will be to make the woman a physical or mental wreck, a jury would be entitled to take the view that the doctor, who under these circumstances and in that honest belief operates, is operating for the purpose of saving the life of the mother, except in the case of a feeble-minded or 'prostitute-minded' woman, both being cases in which pregnancy is unlikely to affect the mind injuriously. The doctor can base his opinion only on knowledge and experience and, if he in good faith thinks an operation to be necessary for the

purpose of preserving the life of the girl in the circumstances set out above, then not only is he entitled to perform the operation but it is also his duty to do so.

The judge went on to say that it was not contended that the words meant merely 'for the purpose of saving the mother from instant death'. If it is reasonably certain that ultimately the mother must die as the result of delivery, the law does not require the surgeon to wait until the woman is in peril of immediate death: in such a case he is not only entitled, but it is his duty, to perform the operation with a view to saving her life. 'So far as danger to life is concerned,' the judge said, 'you cannot of course be certain of the result unless you wait until a person is dead: nobody suggests that the operation only becomes legal when the patient is dead.' Where the duty to operate exists, refusal to do so on so-called religious or other similar grounds may render the surgeon liable to a charge of manslaughter, in the same way that parents may be held liable for the death of their child as a result of their refusal for the same reasons to call in medical aid.

The conclusions, therefore, to be deduced from the case appear to be these:

To be legal the operation must be performed by a qualified medical man in good faith for the purpose only of saving the life of the woman, and 'saving the life' would seem to include 'preventing the patient from becoming a mental and physical wreck so that her life is endangered thereby'. If the surgeon is of opinion, on reasonable grounds and with adequate knowledge, that the probable consequence of a continuance of the pregnancy would be to make the woman a mental and physical wreck, the operation is apparently justifiable as an operation for the preservation of the mother's life, except in the case of a feeble-minded or 'prostitute-minded' woman. When an operation is justifiable on the grounds just stated, the surgeon is not required to wait until the woman is in peril of immediate death, but it is his duty to perform the operation without delay.

Methods of Inducing Abortion

The Use of Oestrogenic Hormones

Preparations of the oestrogenic hormone have been employed experimentally in the attempt to interrupt pregnancy in lower animals. They act by suppressing the luteal phase of the menstrual cycle and inducing another phase which, though not abnormal in itself, is unsuitable for the development of the embryo.

A. S. Parkes *et al.* investigated the effect of two recently evolved oestrogenic substances, ethinyl oestradiol and diethyl-stilboestrol. Rabbits were given orally from 0·25 to 1 mg. of the former and from 1 to 4 mg. of the latter in propylene glycol solution. It was found that small doses of these orally active oestrogenic substances prevented implantation of the blastocyst if given soon (2 to 7 days) after ovulation, or they might terminate established pregnancy.

Available knowledge suggests that the hormone control of the menstrual cycle in primates is the same as in lower animals, so that the conclusions arrived at by Parkes and his co-workers could appear to be applicable to women. The fact, however, that large amounts of oestrogenic hormone are excreted by pregnant women suggests that the period during which oestrogenic therapy might be effective in interrupting pregnancy would be relatively much shorter than in animals.

Elden, C. A. (1938) *Amer. J. Obstet. Gynaec.*, **35**, 648.
Hanley, B. J., and Golenternek, D. (1939) *West. J. Surg.*, **47**, 137.
Holtz, F. (1938) *Acta obstet. gynec. scand.*, **18**, 245.
Parkes, A. S., Dodds, E. C., and Noble, R. L. (1938) *Brit. med. J.*, **2**, 557.
Peters, S. B. (1939) *Minn. Med.*, **22**, 166.
Potter, M. F. (1938) *J. Obstet. Gynaec.*, **45**, 233.

ABORTUS FEVER

See also Surveys and Abstracts 1939, p. 183

TREATMENT

13 Several cases have been reported in which the use of prontosil has given striking results in the treatment of undulant fever. Berger and Schnetz treated a patient with prontosil by mouth; Suchier employed prontosil rubrum; and de Millas gave daily

13 injections of prontosil soluble. In all 3 cases the temperature had fallen to normal within a week and no relapse occurred. Richardson also treated 2 cases; in the first the temperature fell after 6 days' treatment with prontosil album, 0·6 g. twice daily, and an injection of 5 c.cm. of a 5 per cent solution of prontosil soluble on each of 4 consecutive days. In this case symptoms returned after 4 weeks and were relieved by prontosil treatment and no further relapse has since occurred. In the second case the patient's temperature fell after 4 days of treatment. Francis carried out some tests *in vitro* with the organisms recovered from one of his cases; the results of those tests appear to show that *Brucella abortus* was much more susceptible to the action of sulphanilamide *in vitro* than was the pyogenic streptococcus under the same conditions.

Berger, W., and Schnetz, H. (1937) *Med. Klinik*, **33**, 594.
de Millas, W. (1937) *Der Landarzt*, **32**, 423.
Francis, A. E. (1938) *Lancet*, **1**, 496.
Richardson, L. A. (1938) *Lancet*, **1**, 495.
Suchier, W. (1937) *Fortschr. Ther.*, **13**, 305.

ACANTHOSIS NIGRICANS

AETIOLOGY

14 The question whether or not the juvenile and adult cases should be regarded as examples of one and the same disease remains undetermined. Behdjet, analysing a large number of cases of both types taken together, concluded that most cases were not attended by malignant developments and added the argument against a necessary malignant connexion that, in view of the frequency of cancer, the accompaniment of acanthosis should be more common than it is.

Several observers regard endocrine disturbance as a probable cause: thyroid, pituitary and gonads (Behdjet), and adrenal (Gordon) being the glands more commonly affected. Dowling and Freudenthal reported a case with the most unusual accompaniment of tricho-epithelioma, and suggested that the same (unknown) change which produces the epidermal proliferation indicated by the term 'acanthosis' also produces the epitheliomatous proliferation.

Behdjet, H. (1932) *Bull. Soc. franç. Derm. Syph.*, **39**, 192.
Dowling, G. B., and Freudenthal, W. (1938) *Brit. J. Derm.*, **50**, 467.
Gordon, H. (1936) *Brit. J. Derm.*, **48**, 639.

ACCESSORY SINUSES OF THE NOSE

15-17 See Surveys and Abstracts 1939, p. 183.

ACHALASIA

See also Surveys and Abstracts 1939, pp. 43 and 185.

IN THE ALIMENTARY TRACT

Of the Pharyngo-Oesophageal Sphincter

18 *Pathogenesis.*—Etzel extensively investigated mega-oesophagus in Brazil, where it was common among poor people and constantly associated with other morbid conditions, namely, megacolon (in two-thirds of 22 cases), achalasia of the pylorus, achlorhydria (70 per cent of a series), and achalasia in the urinary system leading to the formation of mega-ureter, hydronephrosis, enlarged bladder, polyneuritis, and a low basal metabolic rate. Tissues from 14 necropsies, examined microscopically, showed destruction of Auerbach's plexus and hypertrophy of the circular muscle (but not of the cardiac sphincter) in all, and oesophagitis and leucoplakia of the oesophagus in some. The degeneration of Auerbach's plexus was compared with that produced by B_1 avitaminosis; the author concludes that mega-oesophagus and megacolon, and the associated conditions, are probably manifestations of a chronic deficiency of vitamin B_1.

Course and Prognosis.—Hurst reviewed the reports of the association between the Plummer-Vinson syndrome and carcinoma of the oesophagus. Carcinoma in the neighbourhood of the pharyngo-oesophageal sphincter occurred almost exclusively

in women, probably because it followed the Plummer-Vinson syndrome which was almost unknown in men. Hurst enumerated the various authors who recorded squamous-celled carcinoma of the upper end of the oesophagus associated with dysphagia of long duration, atrophy of the mucous membrane of the tongue and pharynx, cracks at the angles of the mouth, and idiopathic hypochromic anaemia—all of which are characteristic of the Plummer-Vinson syndrome. Ahlbom found that 70 per cent of 153 women with cancer of the mouth, pharynx, or upper end of the oesophagus gave a history suggesting simple achlorhydric anaemia or the Plummer-Vinson syndrome. 18

The diagrams in Vol. I on page 119 (Fig. 27) require modification as achalasia of the cardia is the one condition in which there is no gastric air-bubble. This is due to the fact that the food retained in the oesophagus completely blocks it and prevents the air normally swallowed with food and drink from entering the stomach (see Fig. 1). This fact has never been recorded prior to 1938 (Hurst).

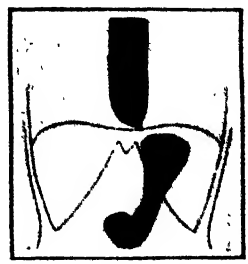


FIG. 1. Achalasia of the cardia, showing absence of gastric air-bubble owing to lock formed by food and saliva permanently filling the lower six inches of the dilated oesophagus. (From the *British Medical Journal*, 1938)

Ahlbom, H. E. (1936) *Brit. med. J.*, **2**, 331.
Etzel, F. (1937) *Guy's Hosp. Rep.*, **87**, 158.
Hurst, A. (1938) *Brit. med. J.*, **1**, 661.
— (1939) *Lancet*, **1**, 621.

ACHLORHYDRIA

See also Surveys and Abstracts 1939, p 185

ACHLORHYDRIA AND CANCER OF THE STOMACH

Hurst brought forward further evidence in confirmation of his previous hypothesis that the achlorhydria present in 65 per cent of cases of gastric carcinoma (i.e. almost all those not secondary to a chronic ulcer) was due to chronic gastritis, both of which might precede the development of the growth. Review of the evidence suggested that carcinoma developed from malignant changes in chronically inflamed gastric mucosa. 19

Hurst, A. (1939) *Lancet*, **1**, 553.

ACKEE POISONING

DEFINITION

Evans and Arnold carried out experiments to determine the toxic principle of ackee and its nature. That it might be a glycoside had been suggested on general grounds, but these investigators separated the saponin, fat, and phytosterol constituents, and demonstrated the toxicity of the saponin. This substance, when extracted from unopened ackees, was haemolytic, but extracts of fully opened ackees were not haemolytic. 22

Evans, K. L., and Arnold, L. E. (1938) *Trans. R. Soc. trop. Med. Hyg.*, **32**, 355.

ACNE

See Surveys and Abstracts 1939, p 185. 23

ACROMEGALY

PATHOLOGY

A. L. Grafflin mentions an unpublished thesis (1916) with illustrations on the normal, the acromegalic, and the hyperplastic nephritic human nephron, as shown in reconstruction models made by Turley. In Turley's model of the nephron in acromegaly, taken from kidneys twice the normal size, the convoluted part of the proximal tubules was greatly increased in length, but the glomeruli were not enlarged as they were in the cases described by Cushing and Davidoff. In Turley's 24

24 reconstructed model of chronic nephritis the outstanding feature was enormous enlargement of the proximal tubules, both pars convoluta and pars recta.

CLINICAL PICTURE

Changes in Bone and Other Tissues

Wakeley and Atkinson recorded a case of acromegaly in a woman aged 21 with excessive enlargement of the tongue and marked prognathism. Radon seeds inserted into the large pituitary tumour found at operation arrested further development of the condition. Later glossectomy and surgical removal of a piece of the mandible were carried out, with excellent results. A second case was reported in a man of 25. Although he enjoyed excellent vision, and no sign of papilloedema was present, the brain, at necropsy, weighed 74 oz. and an enormous pituitary gland had flattened the optic nerves in a huge pituitary fossa. Probably the large size of the latter accounted for the absence of the characteristic eye signs.

Cutis verticis gyrata occurs in conditions other than acromegaly; and, in order to draw a distinction between the congenital and naevoid cases and the giant growth of the scalp in acromegaly, it has been suggested by Parkes Weber that the acromegalic cases should be called 'dermatomegaly of the scalp' and that the title cutis verticis gyrata should remain as a description of the naevoid and congenital cases.

Constitutional Derangements

A case of acromegaly reported by Yealland showed visual fields which suggested that the neurons arising from the nasal halves of both retinae, and from the temporal half of the left retina, had been destroyed by pressure of the growth upon the optic chiasma. Yet when light was thrown on the right retina both pupils contracted normally. This led to the conclusion that the neurons arising from the nasal halves of the retinae do not participate in transmission of impulses concerned in the light reflex.

Courville and Mason, in a report based on the study of 24 acromegalic patients, drew attention to the large number of deaths resulting from heart failure; 15 patients presented evidence of marked heart failure and 6 died from heart failure. Eosinophilic pituitary adenomas were present in all these cases and were associated with marked splanchnomegaly and cardiac enlargement. It was suggested that the hormonal action on the heart was a primary factor in the ultimate production of heart failure, and not the skeletal, muscular, or vascular over-growth, and that the characteristic deformity of the chest and upward displacement of the heart played a minor part only in the cardiac hypertrophy and failure. In two patients with little clinical evidence of acromegaly cardiac failure was the first symptom; characteristic visual fields, and X-ray changes in the phalanges and sella, were later found, and improvement in the cardiac condition followed intensive X-ray therapy of the pituitary.

Courville, C., and Mason, V. R. (1938) *Arch. intern. Med.*, **61**, 704.
Cushing, H., and Davidoff, L. M. (1927) *Monogr. Rockefeller Inst. med. Res.* No. 22.
Grafflin, A. L. (1939) *Arch. Path.*, **27**, 691.
Wakeley, G. P. B., and Atkinson, F. R. B. (1938) *Surgery*, **3**, 8.
Weber, F. P. (1938) *Proc. R. Soc. Med.*, **31**, 1359.
Yealland, L. R. (1938) *Proc. R. Soc. Med.*, **31**, 213.

ACTINOMYCOSIS

See also Surveys and Abstracts 1939, p. 186.

CLINICAL PICTURE

Cervico-Facial Actinomycosis

26 *Infection of tongue.*—The hard 'wooden tongue' of cattle ascribed by Bollinger and others to actinomycosis was shown by Lignières and Spitz (1902) to be due to a Gram-negative bacillus; this infection—actinobacillosis—has been established in only 3 human cases. In genuine actinomycosis, the tongue is attacked in only 3 per cent of cases (Cope, 1938).

TREATMENT

26

Although very large doses of potassium iodide internally—up to 300 grains or more daily—have been advocated, Cope (1938) did not consider that large doses gave better results than moderate quantities, and regarded such large doses as neither necessary nor advisable.

Sulphonamide preparations, though in an experimental stage, have given encouraging results (Cope, 1939).

Cope, Z. (1938) *Actinomycosis*, London.
— (1939) *Practitioner*, **142**, 326.
Lignières, J., and Spitz, G. (1902) *Bull. Soc. cent. méd. vét.*, **20**, 487.

ACTINOTHERAPY

See also Surveys and Abstracts 1939, p. 187.

ARTIFICIAL LIGHT TREATMENT

Physiology

Photo-Sensitizing Effect of Sulphonamide Drugs

27

Hallam reported the case of a man, aged 25 years, who, on January 20th, 1939, had a single ultra-violet light treatment. On January 25th he was admitted to hospital with apparently a very extensive burn of the second degree, a temperature of 102° F., and the history that the inflammation of the skin had followed shortly after the ultra-violet light exposure. The pain necessitated 2 doses of morphine ½ gr., and he was given prontosil album 15 gr., 3 times daily. On January 27th he looked ill; his temperature varied from 100° to 102 8° F.; the whole of the skin of the face was oedematous, red, and covered by brownish-black crusts; the lips were swollen and there were many bullae inside the mouth. The skin of the body was widely and acutely inflamed. It was then found that the patient had, before the ultra-violet exposure, taken one tablet of M & B 693, 3 times daily for 4 days; the prontosil was then discontinued. On January 30th the temperature was normal, and a complete recovery followed.

There appeared to be grounds for assuming that this man's skin was photosensitized by some chemical reaction following the administration of the drug, and that the exposure to a moderate dose of ultra-violet light had precipitated the onset of intense reaction. If this view is correct, every prescriber of a sulphonamide drug should be aware of this possibility, and every patient warned of the danger of exposure to strong or artificial sunlight during the time he is taking this remedy.

Several other reports of a similar nature, attributing to sulphonamide preparations a photo-dynamic effect, have appeared in the literature.

On the other hand, Eidinow has reported that experience at the St. John Clinic and Institute for Physical Medicine indicates that local or general ultra-violet irradiation may be safely applied to patients receiving drugs of the sulphonamide group. He observed 22 patients who were being treated for toxic arthritis, or other conditions, and who received 2 tablets of sulphonamide-P 3 times a day for 10 days (a total of 30 g.). These patients were all exposed to normal sunshine, and to (i) tungsten-arc lamps 10 to 15 minutes twice a week; (ii) the carbon-arc lamp 30 to 60 minutes twice a week; and (iii) the daylight lamp (Eidinow) one hour twice a week. There was no evidence of light-sensitization.

Until further evidence is available it is probably safer to observe caution when giving sulphanilamide to patients who are likely to be exposed to strong sunlight, or who are receiving a course of ultra-violet irradiation.

Eidinow, A. (1939) *Brit. J. phys. Med.*, N.S. **2**, 150.
Hallam, R. (1939) *Brit. med. J.*, **1**, 559.

ADENOIDS

See Surveys and Abstracts 1939, p. 187.

28

ADIPOSITY

See Surveys and Abstracts 1939, p. 188.

29

ADRENAL GLAND DISEASES

See also Surveys and Abstracts 1939, p. 189.

ADRENAL HYPOPLASIA AND INSUFFICIENCY

ADDISON'S DISEASE

Treatment

30 The most important recent advance in the treatment of Addison's disease has been the isolation from the adrenal cortex, and the subsequent synthesis, of desoxycorticosterone and its ester desoxycorticosterone acetate. This substance maintains adrenalectomized animals in good health, and has been shown to be efficacious in Addison's disease (Levy Simpson, 1938); 5 mg. are equivalent to 10 c.cm. of cortin. It is available in ampoules of 5 or 20 mg. per c.cm. of oily solution and is given intramuscularly. Some patients, however, appear to be hypersensitive, as judged by local reactions, which may be so severe as to make continued therapy impossible. Levy Simpson (1939), however, found that desoxycorticosterone acetate was also efficacious by inunction, although 4 times the dose was necessary, or by the subcutaneous implantation of 4 tablets each of 50 mg., the duration of efficacy by this route lasting about 3 months. It is not yet certain that desoxycorticosterone acetate is the only constituent of the crude adrenal cortex extract, cortin.

Thorn, Howard, Emerson, and Firor reported 6 cases of Addison's disease successfully treated by the insertion into the subcutaneous tissue of pellets of crystalline cortical hormone (synthetic desoxycorticosterone acetate). The patients were first injected hypodermically with the hormone in sesame oil daily to measure the daily requirement of the patients, a point on which stress was laid. Pellets of the crystalline hormone, each weighing 50 to 150 mg., were implanted under local anaesthesia in the infra-gluteal region, and were absorbed at a rate of 0·25 to 0·35 mg. a day. No ill-effects were produced; the patients all improved, and were relieved of the necessity for daily injection of the hormone, as absorption continued for a comparatively long time. This method was based on the experimental observations of Deanesly and Parkes. It is necessary to supplement this method of treatment at times of crisis and during the course of an acute infection.

Simpson, S. L. (1938) *Lancet*, **2**, 557.
(1939) *Proc. R. Soc. Med.*, **32**, 685.
Thorn, G. W., Howard, R. P., Emerson, K., and Firor, W. M. (1939) *Johns Hopk. Hosp. Bull.*, **64**, 339.

AEROPHAGY

AETIOLOGY

31 The gas bubble present under the diaphragm and revealed by radiography is derived from the air swallowed with food and drink, the only condition in which it is absent is achalasia of the cardia, in which the contents of the oesophagus prevent the air from passing into the stomach. This air bubble is prevented from abnormally increasing by unconscious silent eructation, and by passage through the pylorus when in the horizontal position. If the normal expulsion is prevented, enormous quantities of gas collect, producing the condition of *aérogastrie bloquée*; this may be caused by spasm of the lower end of the oesophagus set up by an oesophageal ulcer or by dislocation of the cardia, generally due to excess of gas in the splenic flexure.

Hurst, A. (1938) *Brit. med. J.*, **1**, 661.

AGRANULOCYTOSIS

See also Surveys and Abstracts 1939, pp. 177 and 193.

AETIOLOGY

32 The main factors in the causation of agranulocytosis appear to be the synthetic drugs which have profound effects on susceptible persons, although according to Reznikoff (1938) other factors, such as fatigue, worry, and insomnia, also play a part in its onset.

Knowledge of the dangers of the use of amidopyrine together with recent restrictions have reduced considerably the number of cases ascribed to it in the last 2 years. Experiments have shown that patients recovering from agranulocytosis are particularly sensitive to even small doses of amidopyrine (Plum; Israëls and Wilkinson), and patients showing similar sensitivity without symptoms of agranulocytosis have also been described. The subject is very well discussed by Plum, who demonstrated that small doses of the drug given to sensitive subjects will diminish the number of immature granulocytes in the marrow and of the granular cells in the circulating blood.

Cases of agranulocytosis are still reported after the use of gold and arsenical preparations, and less often after the barbituric acid derivatives. The main causes, however, appear to be the newer synthetic drugs used in the treatment of infections with streptococci, gonococci, meningococci, pneumococci, and *Bact coli*. Quite a large number of cases of agranulocytosis, mainly fatal, have already been reported during the last 3 years after the use of drugs, such as prontosil, sulphanilamide, M & B 693 (2-sulphanilyl-amidopyridine) and uleron (dimethyldisulphanilamide), and leucopenia and neutropenia have also been described (Whitby, 1938; and many others). Colebrook recently drew attention to the danger attached to the use of these drugs and concluded that there is not much margin between the amount necessary to control a severe streptococcal infection (20 to 30 g. of sulphanilamide) and that amount (30 to 60 g.) which may initiate an attack of agranulocytosis in susceptible individuals. He emphasized the importance of frequent white-cell counts, especially when the total dosage is 25 g. or more, if the temperature is not showing a prompt response, or if there are any other toxic signs, such as headaches.

PATHOLOGY

Examination of the marrow by sternal puncture shows essentially an arrest of maturation in the granulocyte-producing tissue; the stage at which this occurs and the totality of the arrest depend on the severity of the condition; most commonly it is at the myeloblast stage. In the fatal cases mature and immature granulocytes are absent, whereas erythroblasts are present in normal number and appearance; the longer the clinical course the more marked is the apparent increase in the plasma cells and lymphocytes, but this increase is only relative and is due to eventual diminution, or non-appearance, of myeloblasts. The marrow in agranulocytosis is much less cellular than normal. These changes in the bone marrow precede those seen in the circulating blood and are of prognostic and diagnostic importance (Darling *et al.*; Plum, Israels and Wilkinson).

COURSE AND PROGNOSIS

The mortality is 75 to 80 per cent when no specific, or when inadequate, treatment is given, but the use of pentnucleotide has reduced this to 33 to 35 per cent (Jackson and Tighe). The outlook is always very grave, but if recovery occurs it appears to be permanent and there is little likelihood of relapse provided the sensitizing drugs are not again taken.

TREATMENT

Specific Treatment

Control of the Agranulocytosis

Pentnucleotide is still the most satisfactory form of treatment for the condition (Israëls and Wilkinson; Wilkinson and Israels; Jackson and Tighe) although 1 g. of adenine sulphate intramuscularly 3 times daily (Reznikoff, 1933), yellow bone-marrow or extracts (Giffin and Watkins; Marberg and Wiles, 1938), and transfusions of blood from leukaemic patients of the same group (Ravina; Bock) have all been reported to have given satisfactory therapeutic responses.

Prevention of Relapses

Undoubtedly the most important prophylaxis is discontinuance of the drugs concerned; when this is not possible, the greatest care must be taken in their use – regular blood examinations (particularly total and differential white-cell counts) being made, and administration immediately stopped when the slightest signs of intolerance or toxic reactions, however mild, are noted. Prolonged courses of sulphanilamide should be avoided at all costs.

Bock, H. E. (1937) *Fortschr. Ther.*, **13**, 537.
Colebrook, L. (1939) *Lancet*, **2**, 158.

Darling, R. C., Parker, F., Jnr., and Jackson, H., Jnr. (1936) *Amer. J. Path.*, **12**, 1.
Giffin, H. Z., and Watkins, C. H. (1938) *Minn. Med.*, **21**, 62.
Israëls, M. C. G., and Wilkinson, J. F. (1937) *Quart. J. Med.*, N.S. **6**, 35.
Jackson, H., Jnr., and Tighe, T. J. G. (1939) *New Engl. J. Med.*, **220**, 729.
Marberg, C. M., and Wiles, H. O. (1937) *J. Amer. med. Ass.*, **109**, 1965.
—— —— (1938) *Arch. intern. Med.*, **61**, 408.
Plum, P. (1937) *Clinical and Experimental Investigations in Agranulocytosis with special reference to the Etiology*, Copenhagen.
Ravina, A. (1937) *Pr. méd.*, **45**, 1760.
Reznikoff, P. (1933) *J. clin. Invest.*, **12**, 45.
—— (1938) *Amer. J. med. Sci.*, **195**, 627.
Whitby, L. E. H. (1937) *Lancet*, **1**, 1517.
(1938) *ibid*, **2**, 1095.
Wilkinson, J. F., and Israels, M. C. G. (1934) *Lancet*, **2**, 353.

ALBINISM

34 Waardenburg claimed that carriers of albinism (heterozygotes) show on illumination a transparency of the iris due to deficiency of pigment.

Waardenburg, P. J. (1934) *Report of the 11th Assembly of the International Federation of Eugenic Organizations*, Zurich, p. 44.

ALBUMINURIA

35 See Surveys and Abstracts 1939, p. 194.

ALCOHOLISM

See also Surveys and Abstracts 1939, p. 194.

THE TOXIC EFFECTS OF ALCOHOL

ACUTE ALCOHOLISM

Delirium Tremens or Acute Alcoholic Delirium

36 In delirium tremens the output of urine may be diminished, or there may be incontinence of urine and faeces. Muscular twitchings may occur. Estimation of the blood-urea is a valuable guide in prognosis.

ALKALOSIS

37 See Surveys and Abstracts 1939, p. 198.

ALKALOSIS OCCURRING IN THE ALKALINE TREATMENT OF PEPTIC ULCER

CLINICAL PICTURE

38 At least 16 new cases of alkalosis occurring during treatment with alkali have been reported in Great Britain, the United States, Australia, and China. Practically all the authors lay stress on the importance and danger of renal insufficiency. Cope further analysed the blood changes in several cases of alkali alkalosis; he estimated not only the serum total base, but also the serum calcium and serum magnesium, as the patients who developed this condition were taking an alkaline powder which contained a considerable amount of calcium carbonate and magnesium. He found that, in his patients, the total base was slightly but significantly raised; that the serum calcium was raised considerably above the normal limit; and that the serum magnesium was also raised; the only other condition in which a raised serum

magnesium had been reported in man was nephritis, when magnesium sulphate was being administered as a purgative The conclusion was reached that the accumulation of these inorganic substances might be partly responsible for the functional renal impairment and the resulting severe nitrogenous retention As soon as the excessive intake of these simple alkaline inorganic compounds was stopped, the kidney could restore to normal the calcium, magnesium, and bicarbonate values in the blood

Cope, C L (1936) *Clin Sci*, 2, 287

ALLERGY

See also Surveys and Abstracts 1939, p 198

GENERAL DIAGNOSIS OF ALLERGIC CASES AND IDENTIFICATION TESTS

ALLERGY IN INFECTIVE DISEASES

40

The part played by allergy in infective disease is important A distinction should be drawn between the two groups of phenomena which have been termed allergic (i) The apparently inborn tendency to acquire unusual sensitivity to various antigens which occurs in a small proportion only of the human race and which underlies the so-called 'allergic' diseases, characterized by an immediate reaction on contact with the specific antigen, and by a rapidly developing reaction on skin-testing this is the condition that Coca has called 'atopy (ii) The altered reactivity to certain infective organisms or their products which occurs in any infected animal and profoundly influences the course of the diseases caused by these organisms characterized by delayed reactions to intradermal skin-testing as typified by the cutaneous tuberculin reaction There are undoubtedly many similarities between the two groups, but their exact relation to each other is still largely conjectural The relation of allergy to bacterial diseases has recently been reviewed by Opie He points out that in addition to tuberculosis, streptococcal infections are probably profoundly influenced in their course by allergy and that it is likely that allergic phenomena are important in the course of acute rheumatism, acute glomerulo nephritis, and even pneumococcal pneumonia

ALLERGIC DISEASES

RESPIRATORY SYSTEM

Hay-Fever

41

Treatment Zinc ionization in the treatment of hay fever has had a considerable vogue The technique and the results claimed for it have been described by Franklin (1931), Bailey and Shields, and Shields Bailey and Shields treated 243 patients at St George's Hospital by zinc ionization with satisfactory results in the great majority of cases, 93 6 per cent were completely or considerably relieved 5 per cent showed some improvement, and 1 4 per cent no improvement The ages ranged from 5 to 77 years and most of the patients had received other forms of treatment in previous years with no benefit The method they used was that described previously by Shields The nose was sprayed with a 2 per cent solution of cocaine hydrochloride before the treatment Otherwise the method was similar to that originally described by Franklin (1931) The nose was packed with ½-inch ribbon gauze soaked in a 2 per cent solution of zinc sulphate Both sides of the nose were treated simultaneously The current was applied by a 'pantostat', the milliamperage varying from 2 to 20 according to the reaction of the patient Each treatment usually lasted 10 minutes Franklin in 1938 reported on the results of a follow-up of 639 patients treated by this method The results indicated that the treatment was beneficial in a large number of cases, that the best results were obtained from treatment just before or at the onset of symptoms, and that the most effective strength of current was 6 to 10 milliamperes The treatment is clearly palliative only, and produces its effects by local destruction of the reacting tissue, the effect has been compared by Rackemann with that of cauterization of the mucosa

Bloom suggests that allergy is predominantly a disturbance of electrolyte metabolism associated with some endocrine dysfunction, perhaps adrenal in origin He obtained striking benefit from the use of potassium salts (5 grains of potassium chloride three times a day) in 29 cases of hay-fever, the degree of relief in all cases

41 being estimated as over 50 per cent, and in most of them approximating to 100 per cent. These salts are also used in urticaria, eczema, migraine, and chronic allergic sinusitis. No complications were noted.

ALLERGY OF THE SKIN

Urticaria

43 The administration in urticaria of a diet rich in potassium and poor in sodium has been suggested by Rusk and Kenamore, who reported 6 cases showing favourable results. In a condition which so often becomes intractable to the accepted forms of treatment, this measure is worthy of trial.

SERUM SICKNESS AND ACCIDENTS OF SERUM THERAPY

51 *Hypersensitiveness* - There has recently been a tendency to emphasize the frequent discrepancy between the results of skin tests and symptoms As the result of tests on both asthmatic and control subjects, Bruce Pearson concluded that such tests were a source of subsidiary information, to confirm suspicions based on the history; he found that sensitivity to more than one extract was frequent, and that it was exceptional to find subjects highly sensitive to one substance only.

Bailey, I. D., and Shields, C. (1937) *Brit. med. J.*, **1**, 808.
Bloom, B. (1938) *J. Amer. med. Ass.*, **111**, 2281.
Franklin, P. (1937) *Brit. med. J.*, **1**, 1115
(1938) *ibid.*, **1**, 948
Opie, T. L. (1936) *Medicine, Baltimore*, **15**, 489.
Pearson, R. S. B. (1937) *Quart. J. Med.*, N.S. **6**, 165
Rackemann, F. M. (1938) *Arch. intern. Med.*, **61**, 144
Rusk, H. A., and Kenamore, B. D. (1938) *Ann. intern. Med.*, **11**, 1838.
Shields, C. (1936) *Practitioner*, **136**, 645

ALZHEIMER'S DISEASE

54 See also Surveys and Abstracts 1939, p. 202.

AMENORRHOEA

55 See also Surveys and Abstracts 1939, p. 202.

AMOEBIASIS

AMOEBIC DYSENTERY

PROTOZOOLOGY AND PATHOLOGY

***Entamoeba histolytica*: Life History**

56 In an investigation of the morbid changes in tissues invaded by the *E. histolytica* Westphal failed to find any evidence of toxicity, and concluded that proteolytic ferments facilitating the process of invasion were produced. *E. histolytica* pathogenic to cats were found by Awakjan in 5 per cent of Moscow rats and might possibly be a source of human infection

Experiments by Swartzwelder showed that the amoeboid trophozoites of *E. histolytica*, when administered orally, infected 5 of 13 dogs, with an incubation period of 3 to 24 days As free hydrochloric acid of the same strength as that in the stomach did not destroy them within one hour, it therefore appeared that forms other than the encysted might be infective

Various factors influencing the cultivation and pathogenicity of *E. histolytica* have been investigated by Deschiens, he found (1935) that cultures lost their pathogenicity to kittens after cultivation for 90 to 220 days with 5-day transfers. According to Dopter and Deschiens (1936) the addition of normal human serum to a horse-serum culture slope increased the growth of the amoebae 5-fold, whereas the serum from a case of amoebic dysentery produced only 2·57 times as much growth. Bilirubin stimulated the growth of the amoebae and was ingested by them (Deschiens, 1938, a), but bile in a concentration of 1 in 1,000 checked growth and in

1 in 100 killed all the amoebae (Dopter and Deschiens, 1938). Moreover, the addition of a pathogenic strain of *Bact. coli* to cultures of *E. histolytica* increased the infections of cats from 20 to 45 per cent (Deschiens, 1938, b); this factor might influence the susceptibility of human subjects to amoebic infections.

In addition to the common form of *E. histolytica* which forms cysts with a diameter of more than 12μ, a smaller form with cysts of from 5μ to 10μ was not uncommon in the stools. In the Chicago water-borne hotel outbreak they were investigated by Spector, who found them less pathogenic to kittens, both on oral administration and on injection into the rectum.

Wagner, as the result of 8 years' experiments on cats and dogs with the same cultivated strain of *E. histolytica*, found great variations in the susceptibility to infection, which were not due to loss of virulence. Young animals were most susceptible, although in the human subject amoebic dysentery was uncommon in children, probably because of their lesser exposure to infection. The susceptibility of animals was also greater in hot weather; this might account for the greater prevalence and severity of the disease in hot climates.

The Ulcerative Condition engendered by *E. histolytica*

Spector found that the smaller form also produced milder infections in man. Frye and Melency arrived at a similar conclusion as regards amoebae developing from the small cysts, for, when injected into the terminal ileum in kittens, they often failed to infect, and showed less tendency than the large form to invade the mucosa.

DIAGNOSIS

Wilkinson concluded that chronic amoebiasis was often diagnosed as chronic appendicitis, and reported 2 cases treated by appendicectomy; symptoms continued, however, and later *E. histolytica* were found in the stools. Banerji *et al.* reported that *E. histolytica* were found in scrapings of the mucosa in 475 appendicectomies, and that in nearly half of these there was a history of previous dysentery. Cancer of the colon has been reported in 4 patients, 3 to 10 years after suffering from amoebic dysentery.

Craig and Swartzwelder obtained positive reactions with the complement-fixation test in monkeys infected with the *E. histolytica*, but Paulson and Andrews recorded numerous falsely positive reactions with Craig's test; it was therefore unreliable in individual cases, and not so useful in diagnosis as examinations of the stools.

TREATMENT

Emetine. -The toxicity of emetine was discussed by Mattei, who confirmed its cumulative action, as shown by the continued excretion of the drug 40 days after full doses. Of 66 cases of poisoning with the drug, 16 proved fatal; 15 of these had received more than 1·0 g. To avoid danger a watch should be kept for the following premonitory symptoms: persistent nausea or the return of diarrhoea, slight albuminuria, grave hypotension, and increased cardiac response to effort. He advised 0·08 g. daily for 5 days, and after four days' interval 0·06 g. daily for 4 days, or a modified course of 0·06 g. daily for 4 to 7 days.

Arsenic compounds. -- The first fatality after carbarsone was reported by Epstein, after 5 g. given in 10 days during the patient's last course of treatment. Tubular nephritis and fatty degeneration of the liver were found at necropsy.

Chopra *et al.* reported cures in the proportion of 5 out of 6 cases of chronic amoebic intestinal infections from the use of 0·25 g. twice daily of amibiarson, a preparation closely allied to carbarsone.

Liver therapy. --Faust and Swartzwelder recorded beneficial effects from the oral administration of raw liver and of powdered liver extract in the treatment of experimental amoebic infection in dogs, but intramuscular injections were much less effective.

AMOEBIC LIVER ABSCESS

PROGNOSIS

In Indo-China, according to Huard, Long, and Graziani, patients with liver abscess show bacterial infection more often than in India and other tropical countries, and are attended by the very high mortality of 80 to 90 per cent, as compared with 12 per cent in the army in India.

VINYL ETHER

Vinyl ether (divinyl ether), $(CH_2 : CH)_2O$, has also a wide field of usefulness, differing from that of cyclopropane. It is specially well adapted for providing anaesthesia for short operations. It can in fact well replace ethyl chloride and act as a substitute for nitrous oxide when for any reason this is unsuitable.

Unlike cyclopropane, vinyl ether can be given by the simplest of means though its great volatility makes it unwise to administer it by open mask and drop-bottle. However it is given, vinyl ether must be freely diluted with air or oxygen. Great care therefore is needed when it is given from a closed apparatus, such as Clover's.

Action

Vinyl ether produces anaesthesia very rapidly, generally within a minute with the open method of administration. Within about 2½ minutes there is usually sufficient relaxation to allow of laparotomy. Since vinyl ether is rapidly eliminated, there is a quick return to consciousness when administration ceases. A small amount only is required for the induction of anaesthesia. In animal experiments it has been found that respiratory failure occurs before cardiac failure.

The anaesthetic effect of vinyl ether is said to be due to its solubility in fluids. It does not interfere with liver function, and evidence of liver damage has been found only in a few cases after prolonged administration. Wesley Bourne has shown experimentally that, in dogs, it does not enhance liver damage produced by chloroform, nor alter the function of the liver. The risk of such damage is small since vinyl ether is chiefly employed for short anaesthesias.

The ratio of the anaesthetic to the lethal dose of vinyl ether is 1 : 2·4, whereas with ethyl ether and chloroform it is 1 : 1·5. Because of the rapid action of vinyl ether, however, special care to avoid overdosage should be taken, but, because of the rapid recovery rate, care must also be taken to maintain an even level of anaesthesia. Profuse salivation may occur, but this can generally be prevented by the pre-anaesthetic use of atropine. Post-operative nausea and vomiting seldom occur, and pulmonary complications are rare.

Advantages

Vinyl ether produces excellent muscular relaxation, comparable to that by chloroform, and perhaps better than that by ethyl ether. It has not the irritant effect of the latter on the respiratory tract, and so may be employed in lung conditions in which ethyl ether is contra-indicated. Its rapid action, and the readiness with which a change-over can be made to ethyl ether, has led to its use by some anaesthetists in the induction of anaesthesia.

It does not cause cardiac depression as does chloroform, and the risk of post-operative liver damage and acidosis is negligible. The recovery period is more pleasant than that from ethyl ether or chloroform. Its use as an adjunct to nitrous oxide or ethylene does not increase the tendency of these gases to produce anoxaemia.•

Disadvantages

Its rapid action and the low concentration necessary for the production of anaesthesia may lead to too high a concentration in the blood, unless care is taken in its administration. Its odour is objected to by some patients, but can be masked by the addition of eau-de-Cologne.

Uses

For short operations on children vinyl ether may be regarded as the best available inhalation anaesthetic. Nitrous oxide is often inconvenient for these patients, and ethyl chloride is not without risk. Vinyl ether has been extensively used with success for dental operations on the young. It is also very conveniently used in major surgery to reinforce continuous nitrous oxide and oxygen when relaxation is required. It is also employed in otorhinolaryngology, e.g. for tonsillectomy and myringotomy; in ophthalmology for fundus examinations in children; in orthopaedics for manipulation of bones and joints; and in obstetrics for inducing anaesthesia during labour.

Administration

When it is desired to give vinyl ether for operations requiring something more than the single dose sufficient for dental and other quite short procedures, but not

needing continuous gas and oxygen supplemented by vinyl ether, the apparatus designed by Kaye of Melbourne renders easy the continuous administration of vinyl ether and oxygen. The apparatus is not complicated or massive, but provides a flow meter and carbon dioxide absorption. Good results have followed the use of an anaesthetic mixture consisting of 25 per cent vinyl ether and 75 per cent ethyl ether.

The stage of induction is short, anaesthesia occurring in 40 to 60 seconds, and preceded by a brief period of excitement. Breathing is somewhat shallow and rapid during anaesthesia, but the respirations are smooth and equal in volume. A slight flushing of the face is usual, but there should be no cyanosis. Concerning the eye-signs, the eyelids and recti muscles of the globe are slow to relax: the palpebral and conjunctival reflexes disappear, but the pupillary reactions are irregular, and the pupils repeatedly change in size. There is often sufficient muscular relaxation for operating while the lid and eyeball are still moving. The eyeballs oscillate even during deep anaesthesia. Recovery is rapid, compared with ethyl ether or chloroform, and is as rapid as after gas and oxygen. There is rarely excitement, and very rarely nausea or vomiting.

SPINAL ANAESTHESIA

Scope and Limitations

Mention must be made of the application of spinal analgesia to thoracic surgery; for certain lobectomies and thoracoplasties it is regarded as the method of choice.

Technique

Stovaine and Novocain

The 'feel' of the needle. Vol. I, p. 492, line 20 The new sentence should begin 'In the young, injection is easy. . . '.

Etherington Wilson Technique

In the Etherington Wilson technique, which is as warmly recommended by some as it is decried by others, and which was designed after much experiment with coloured solutions and glass tubes, a hypobaric solution of percaine is introduced into the cerebrospinal fluid at the third lumbar interspace, the patient being in the sitting posture which is maintained for a timed number of seconds according to the height of the desired anaesthesia. The patient is then placed on his back, and the table tilted to a measured amount of Trendelenburg inclination. Preliminary injection of scopolamine hypodermically is recommended by the author of the method.

EPIDURAL INJECTION

Dogliotti's innovation of epidural injection, whereby the injected anaesthetic solution does not enter the spinal canal but bathes the roots after they leave the cord, has found few followers in Great Britain. It has been a good deal practised in America without apparently arousing enthusiastic support. Injection through the sacral hiatus into the thecal canal is practised with success for operations on the perineal regions and groins.

RECTAL ANAESTHESIA AND BASAL NARCOSIS

Basal Narcosis

Premedication

Recent years have seen an enormous increase in the employment of barbituric compounds in association with anaesthesia. They are used both in preliminary medication, and as basal narcotics, or as anaesthetics *per se*. For preliminary medication nembutal is probably the most widely used, one capsule being given the night before and 2 an hour before operation. This oral administration of the drug usually brings the patient to the operating table either unconscious or at least in a drowsy indifferent unalarmed state of mind. The effect, however, is not so certain as if the drug is given intravenously. Some anaesthetists prefer this, and give the nembutal as a basal narcotic half an hour or so before operation.

The two other popular barbiturates, evipan and pentothal, if used in association with other anaesthetics are given intravenously just before the main anaesthetic is to be administered. Their action is rapid, and their effect not long-lasting. They are much used by themselves as anaesthetics for short operations. The pleasantness of induction of unconsciousness and the simple technique must not lead anaesthetists to replace by these agents nitrous oxide whenever this meets the case, for there is no

comparison between nitrous oxide and the barbiturates as regards freedom from risk. Moreover, after all the barbiturates, there is the chance of prolonged restlessness and excitement such as is never seen after 'gas'.

Barbiturates are not always the best form of premedication. There is at the moment too great a tendency among anaesthetists to adopt some favourite form of premedication or basal narcotic, and to employ it as a routine without reflecting on the exact object of premedication in the particular case. Premedication and basal narcosis offer immense advantages, but these are only fully reaped if they are given according to a precise idea of the physiological action involved, and of the object in view. For example, one great advantage of suitable premedication is that it enables the safe anaesthetic, nitrous oxide, to be used efficiently on patients who otherwise would have to be submitted to the action of anaesthetics which are tissue poisons. This is brought about by using as the basal narcotic a drug or drugs which lower the basal metabolism. This lowers the oxygen need of the patient, and thus the anaesthetic nitrous oxide which must be given with limited amounts of oxygen is enabled to fill the bill perfectly well. In such a case a full dose of omnopon and scopolamine, or a smaller dose of these and an injection of avertin, is the proper premedication, and is superior to any barbiturate in bringing about the quiet breathing desired. Such a condition is wanted, for example, in upper abdominal operations when deep anaesthesia is necessary and when this without premedication leads to vigorous action of the diaphragm, and intercostal paralysis resulting in an abdominal heave which is exactly what the surgeon most dislikes.

Barbiturates on the other hand are admirably adapted to eliminating in the patient that psychic element which may play so obnoxious or even disastrous a part in anaesthesia. Ventricular fibrillation is known to have a predisposing factor of adrenal hyperactivity as well as the precipitating factor of surgical or other stimulus. Emotional disturbance is a prime cause of adrenal hyperactivity, and thus it is that by obviating emotion the barbiturate or other suitable sedative lessens the risk of fibrillation. Moreover, fibrillation is not the only phenomenon that the anaesthetist fears in really nervous or apprehensive subjects. These people react unfavourably to their anaesthetic not only during the initial stages but throughout the operation, when they are disposed to muscular contraction and movement to an extent quite absent from the naturally placid individual. These awkward tendencies are also greatly controlled by due preliminary medication.

Another fact often overlooked when the preliminary drug is chosen is that atropine is a metabolic stimulant, and should therefore not be given before gas and oxygen. The chief aim of preliminary medication and basal narcosis besides those which have been mentioned is to enable the patient to be efficiently anaesthetized with the comparatively harmless gaseous anaesthetics, nitrous oxide and cyclopropane. Obviously care must be taken that this object is achieved without injurious effects due to the preliminary drugs themselves. Want of this care has led to condemnation of preliminary medication and to the attribution to it of pulmonary after-effects which arise not from its use but from its abuse.

Pentothal Sodium

Pentothal sodium is closely related to nembutal (sodium ethyl methylbutylbarbiturate) and to sodium amytal (sodium isoamylethylbarbiturate).

Pentothal sodium is a lemon-yellow powder, readily soluble in water, its solutions being alkaline in reaction, and having a faint greenish-yellow colour. If solutions do not become perfectly clear, or contain an insoluble residue, after a few seconds, they should be discarded. The drug is supplied in ampoules containing 0·5 and 1 g. of the powder, together with ampoules containing 10 and 20 c.cm. chemically pure sterile water, for dissolving 0·5 and 1 g. respectively of the powder to make a 5 per cent solution. Pentothal sodium is generally given by intravenous injection. The 10 per cent solution is now rarely used.

Action

Pentothal sodium powerfully depresses the respiratory centre, affecting the amplitude rather than the rate of respiration. Overdosage from too rapid administration, or from excessive amounts readily produces cardiac, hepatic, and cerebral damage, from anoxia. Cyanosis is never a troublesome factor. Laryngospasm, trismus, sneezing, coughing, and hiccup occasionally occur, even during deep anaesthesia. Prevention and relief are readily obtainable by the injection of atropine. Where severe overdosage is avoided and oxygenation is adequate, toxic effects

on the circulatory system are negligible. There is generally a fall in blood pressure, though this is rarely marked. When properly administered pentothal sodium causes little change in the pulse-rate.

The drug is destroyed in the liver, and, for this process, an adequate reserve of glycogen is necessary. There is no real evidence that harmful effects on the liver have occurred.

With regard to the kidneys, neither the normal nor the nephritic kidney is adversely affected, and renal disease is not a contra-indication to the use of the drug.

Advantages

The induction stage is rapid and pleasant, and there are rarely nausea and vomiting on recovery. The element of psychic shock is obviated, and patients take pentothal readily for subsequent anaesthetics. The use of narcotics for the relief of pain and restlessness for the first few hours after operation is minimized, and is often unnecessary. Post-anaesthetic nursing is reduced to a minimum.

Disadvantages

The use of pentothal for deep anaesthesia is, in inexperienced hands, not as safe as ether, because the anaesthetist has to depend on a type of respiration characteristic of the drug. The anaesthetist must therefore be familiar with this type of breathing, if it is to serve as a guide to the depth of anaesthesia. The action of pentothal varies greatly in different patients, and even in the same patient at different anaesthesias. Since premedication is necessary, pentothal is not well suited to emergency abdominal operations. Being administered intravenously, its use may be difficult or even impossible in patients with small veins.

Uses

Pentothal sodium may be employed as a total anaesthetic; for rapid and pleasant induction of anaesthesia preliminary to the use of ether or gas; as a basal narcotic, particularly in gas anaesthesia, as a supplement to local or spinal analgesia, especially where the latter is imperfect; in essential hypertension, for estimating the probable value of surgical treatment; as a therapeutic measure for combating the toxic effects of local anaesthetics; for use in convulsive states such as strychnine poisoning, tetanus, and eclampsia; and as a sedative in maniacal states and narcoanalyses (Marshall).

Pentothal sodium is generally given intravenously, though it may be administered orally or rectally, particularly in obstetrics. Given intravenously as a basal narcotic it greatly facilitates the administration of nitrous oxide and oxygen, allowing adequate anaesthesia without suboxygenation Used thus it also allows of economy with the use of cyclopropane which is an expensive gas

Pentothal sodium is indicated for minor and short operations; operations on the face, head, neck, and upper chest; in operations in which the use of the cautery, or diathermy, might lead to ignition of inflammable gases; in orthopaedic operations for the removal of adhesions, and reduction of fractures and dislocations, in minor urological procedures such as cystoscopy, ureteral catheterization, lithotrity, passage of sounds; in ophthalmic surgery; in minor otorhinolaryngological procedures such as myringotomy and antral puncture; in short dental and oral procedures; in minor neuro-surgical procedures, such as lumbar puncture; for nervous and mental patients who fear an anaesthetic mask, as a sedative in maniacal states; for patients suffering from acute diseases of the throat, bronchi, and lungs, such as coryza, bronchitis, early pneumonia, and early pulmonary tuberculosis; to combat convulsive attacks, as in strychnine poisoning; as a basal narcotic or adjuvant to other agents, in most major surgical operations, other than those on the upper part of the abdomen; for bronchoscopy and oesophagoscopy to alleviate distress, and in cases in which there is need for reduction of more potent and toxic supplementary anaesthetics; and for the production of anaesthesia during labour.

Contra-indications

The contra-indications to the use of pentothal sodium are chiefly referable to the depressant effect of large doses on the respiration, and to the probable state of the hepatic function. The absolute contra-indications, which are few, depend largely on the availability or otherwise of facilities for resuscitation, particularly the administration of oxygen. The drug should not be used in advanced pulmonary diseases, or in conditions causing mechanical obstruction in the respiratory apparatus.

It should be used cautiously in operations on the larynx and pharynx, because the

throat reflexes remain active in most patients, even under deep anaesthesia. Most authorities agree that pentothal is detoxified by the liver, and should not be used in advanced disease of that organ. Starvation from trismus or pyloric obstruction, leading to a low glycogen reserve, contra-indicates its use, as does also uncontrolled diabetes mellitus, which connotes a low glycogen reserve. Extreme renal impairment may be a contra-indication. The drug should not be used for operations on the upper part of the abdomen, since respiratory depression will hinder the introduction of supplementary agents. Severe cardiac decompensation, coronary disease, myocardial degeneration and low blood pressure are contra-indications, as are also severe toxaemia and pyrexia which may gravely impair cardiac and hepatic functions. Obese myxoedematous and extremely ill patients are not good risks.

It should not be employed in severe anaemia, since in this condition the oxygen-carrying capacity of the blood is impaired. Long operations with the patient in the sitting position contra-indicate its use. Children under 10 years of age do not tolerate it well, because of their susceptibility to respiratory depression. If sulphanilamide has been given, there is an increased risk of sulphaemoglobinaemia.

Premedication

This is necessary because, in cases with associated pain much larger doses are required to produce the desired effect if premedication is not given. In the attempt to keep the patient quiet an overdose may result.

Ideas with regard to premedication vary. S. V. Marshall holds that premedication is unnecessary for very brief and superficial procedures; that atropine is essential, and morphine advisable, in the more lengthy procedures, especially when pentothal is to be the only anaesthetic. The doses recommended are: atropine, $\frac{1}{150}$ to $\frac{1}{100}$ gr. (0·4 to 0·6 mg.), morphine, $\frac{1}{4}$ to $\frac{1}{3}$ gr. (0·01 to 0·016 g.). Atropine is essential, and morphine optional, when pentothal is to be used for basal narcosis. Morphine is best omitted in intra-abdominal work, since it favours the earlier onset of respiratory depression. Doses: atropine $\frac{1}{150}$ to $\frac{1}{100}$ gr. (0·4 to 0·6 mg.), morphine $\frac{1}{8}$ to $\frac{1}{6}$ gr. (0·008 to 0·01 g.). If vomiting is likely, morphine should be replaced by diamorphine $\frac{1}{12}$ to $\frac{1}{8}$ gr. (0·005 to 0·008 g.). Hyoscine should be avoided. The use of other barbiturates is undesirable, tending to increase restlessness, and possibly to have cumulative effects. Some authorities, however, employ one of the more slowly acting barbiturates, such as sodium amytal or nembutal. Premedication should be given at least an hour before the anaesthetic.

Technique of Administration

Administration of pentothal sodium is by fractional or intermittent injections. The amount necessary to produce anaesthesia varies greatly in different patients, and often in the same patient at different operations. In general, young, active or nervous patients will require more than the old, placid or cachectic. The same variation often applies to the maintenance dose. The drug has a cumulative effect, the longer the anaesthesia the less amount of the drug being necessary to maintain anaesthesia. The injection of pentothal sodium is made at the rate of about 1 c.cm. of the 5 per cent. solution every 5 seconds, the patient being asked to count slowly. When he ceases counting, the amount of solution injected should be noted, and half as much again as has been injected given. After half to one minute relaxation is generally complete, and the operation may be begun. This amount will generally allow of an operation lasting a few minutes. If a longer anaesthesia is required, the needle should be kept *in situ*, and supplementary injections of 0·25 to 1 c.cm. given as required. These supplementary injections required will become progressively smaller and less frequent as the anaesthesia proceeds.

Course of Anaesthesia

The chief characteristic of the anaesthesia is the type of respiration, which becomes progressively shallower with the depth of anaesthesia. Soon the jaw relaxes, and the tongue falls back, causing respiratory obstruction which may be easily overlooked owing to the speed with which this stage is reached. Throughout anaesthesia the chin must be supported firmly in order to maintain a clear airway. The absence of congestion in the nasal passages enables the mouth to be completely occluded in oral procedures. Lightness of anaesthesia is indicated by the increasing depth of respiration. Obstruction, however, will also increase respiratory efforts. Slight movements, phonation, and frowning are other signs of the lightness of anaesthesia. If anaesthesia is deep enough the corneal reflex is either sluggish or absent, the eyeballs are fixed, the eye-lids are flaccid, and the pupils are contracted or semi-dilated.

and react to light. If the airway is clear, the colour remains good, in spite of the shallow breathing, but if there is cyanosis, this connotes either severe respiratory depression or respiratory obstruction. In such circumstances any obstruction should be removed, and coramine injected. Inhalation of saliva, blood, or vomited matter, or the attempt at tracheal intubation may lead to a persistent laryngospasm. Intratracheal insufflation of oxygen should be made.

The time of recovery from pentothal sodium is roughly proportional to the amount of the drug administered. Prolonged unconsciousness is generally due to overdosage or delayed elimination. If post-anaesthetic depression appears to be deep, 5 to 10 c.cm. of coramine should be given intravenously, and repeated if necessary.

Complications

Complications are comparatively rare during and after pentothal anaesthesia, and are generally of minor degree. Vomiting is rare.

POST-ANAESTHETIC COMPLICATIONS

Vomiting

Treatment

The replacement of chloroform and ether by less toxic vapours has done much to reduce the frequency and violence of post-operative vomiting. Yet this remains a formidable foe to the patient's comfort after operation, and mention must be made of a recent treatment which is founded on physiological reasoning and has shown success in practice. This is the use of insulin and glucose as both a preventive of, and cure for, sickness. Two ounces of glucose are given 3 hours before operation, and 5 units of insulin hypodermically half an hour before. The insulin is repeated after operation, and 4 hours later 4 ounces of glucose are given per rectum.

Kaye, G. (1938) *Med. J. Aust.*, **2**, 856.
Marshall, S. V. (1939) *Med. J. Aust.*, **3**, 382.
Wilson, W. F. (1934) *Brit. J. Anaesth.*, **11**, 43.
(1936) *ibid.*, **13**, 108.

ANEURYSM

See Surveys and Abstracts 1939, p. 213 **61**

ANGINA PECTORIS AND CORONARY THROMBOSIS

See also Surveys and Abstracts 1939, p. 215.

CORONARY THROMBOSIS

CLINICAL PICTURE

Complications

To the complications mentioned in Vol. I, p. 569 two more may be added, namely perforation and cardiac aneurysm **62**

Perforation

Perforation of the inter-ventricular septum rarely occurs at the site of an infarction.

Cardiac Aneurysm

Cardiac aneurysm also occurs, especially from an anterior infarction, it can be recognized by radiological and clinical signs (Parkinson, Bedford, and Thomson): there is expansile systolic pulsation apart from the apex beat; the heart is enlarged to the left and deformed; adhesions are present between the heart and the chest or diaphragm, and the wall of the sac may be calcified. The contained clot may be the origin of an embolus.

Changes in the Electrocardiogram

In addition to the changes in the 3 leads described in Vol. I, p. 569, changes have now been recorded in lead IV (the chest lead); these changes may in fact precede those in the other leads and remain in the late stages when the other changes are no longer seen.

62

TREATMENT

Diet.—The value of a low calorie diet is becoming increasingly recognized. For the first week at least, fluids only should be given: the Karell diet consists of 200 c.cm. of milk 4 times daily at intervals of 4 hours, with, if necessary, 200 c.cm. of water.

Bedford, D. E. (1939) *Trans. med. Soc. Lond.*, **62**, 165.
Parkinson, J., Bedford, D. E., and Thomson, W. A. R. (1938) *Quart. J. Med.*, N.S. 7, 455.

ANGIO-KERATOMA

63 *Treatment*

Pastorino recorded a 'cure' in a girl of eighteen treated with oestrone (progynol). The patient showed signs of deficiency of ovarian hormone, and this treatment resulted not only in restoring menstruation but also in ameliorating the angio-keratoma.

Pastorino, M. (1937) *Ann. Derm. Syph., Paris*, 7e ser., **8**, 90.

ANGIOMA

See also Surveys and Abstracts 1939, p. 218

PROGNOSIS

64 The very pale pink mark occurring in very young babies on the forehead, the nape of the neck, alae nasi, and occasionally elsewhere, disappears spontaneously when the child is about a year old. Lister showed that a number of cavernous angiomas involving the skin as bright red marks and growing rapidly in the early months disappeared in about 5 years, a few cases, however, conformed to Lister's description except that they did not disappear without treatment. Capillary angiomas did not tend to disappear.

TREATMENT

The above observations considerably increase the difficulty of decision about the treatment. Probably the safest plan in the case of angioma in unimportant situations is to wait, at any rate until the child is one and a half to 2 years old. But for angioma on the face radium treatment, which does not cause scarring, must be regarded as the safest method. In the presence of any tendency to spontaneous ulceration and this is not uncommon radium, used with the utmost care and circumspection, is indicated. This discovery emphasizes the condemnation of methods which cause scarring. Patients now are not treated before the age of 3 months because of the risk of failing to recognize the undeveloped part of the angioma, which subsequently develops around the cured area. Great care must be taken to treat the subcutaneous portion.

Lister, W. A. (1938) *Lancet*, **1**, 1429.

ANKYLOSTOMIASIS OR HOOKWORM DISEASE

66 See Surveys and Abstracts 1939, p. 218.

ANOREXIA NERVOSA

See also Surveys and Abstracts 1939, pp. 45 and 219.

AETIOLOGY AND CLINICAL PICTURE

67 A discussion on anorexia nervosa took place at the Royal Society of Medicine in January, 1939. The fallacy of attributing the condition to an endocrine dysfunction was stressed by Ryle, Sheldon, Spence, and Yellowlees. The symptoms were often formerly, and in Germany still are, considered to be an expression of Simmonds's disease, but actually there is no connexion between the two diseases. Sheldon noted the similarity between anorexia and starvation as it occurs in times of famine,

comparing especially the growth of hair on the face and of downy hair on the trunk and limbs which occurs in both conditions. Spence suggested that the diminished food intake might lead to a deficiency of vitamins, especially E but possibly also A, sufficient to affect the endocrine glands, though not severe enough to cause gross symptoms of deficiency. Several speakers discussed the significance of amenorrhoea and agreed that this could not be a result of the starvation, as it often preceded the anorexia nervosa: it must be considered as a primary functional amenorrhoea, probably psychological in origin. 67

Ryle, J. A., Sheldon, J. H., Spence, A. W., Hurst, A., Patterson, S. W., Yellowlees, H., and Weber, F. P. (1939) *Proc. R. Soc. Med.*, **32**, 735.

ANTENATAL CARE

See also Surveys and Abstracts 1939, pp. 29 and 219.

THE OBSTETRICAL EXAMINATION

An improved form for antenatal records is now in use at University College Hospital (see Plate opposite). The chief changes in this form are (i) a more detailed record of the general medical examination; and (ii) a column for records of weight at each consultation: this is now regarded as important in regard to early diagnosis of toxaemia of pregnancy (see Vol. X, p. 97). 68

ANUS DISEASES

See also Surveys and Abstracts 1939, p. 220.

ANO-RECTAL FISTULA

Definition

The classification of fistula suggested by Milligan and Morgan, now widely recognized as a practical simplification, is as follows: (i) subcutaneous and submucous fistulae; (ii) fistulae with main tracks entering the anal canal *below* the ano-rectal ring (anal fistulae): (*a*) low-level anal fistula, and (*b*) high-level anal fistula; (iii) fistulae with tracks extending *above* the ano-rectal ring (ano-rectal fistulae): (*a*) with internal openings into rectum, (*b*) without internal openings, and (*c*) with main-track openings into the anal canal below the ano-rectal ring. 71

PRURITUS ANI

Aetiology

A fungus infection may be responsible for pruritus ani. The mycotic infections may be caused by the epidermophyton, or yeasts of the type known as *Monilia albicans*. Clinically a mycotic cause may be suspected when a localized dermatitis is found round the anus with a well-defined circumscribed edge.

Treatment

Treatment is usually by local applications of Castellani's carbol fuchsin paint, or by 1 or 2 per cent gentian violet in 20 per cent alcohol.

Milligan, T. T. C., and Morgan, C. N. (1934), *Lancet*, **2**, 1150, 1213.

APHTHOUS FEVER

TREATMENT

Treatment of stomatitis with 1 per cent aqueous solution of gentian violet was recommended by Ebbs. Symptoms sometimes subsided after one application and the only disadvantage of the method was the temporary discoloration caused. 73

Ebbs, J. H. (1938) *Arch. Dis. Childh.*, **13**, 211.

APPENDICITIS

See Surveys and Abstracts 1939, p. 221. 75

ARGYLL ROBERTSON PUPIL

See Surveys and Abstracts 1939, p. 222. Vol. II 77

ARRHYTHMIA

78-85 See Surveys and Abstracts 1939, pp. 59 and 223.

ARTERIAL DISEASE AND DEGENERATION

86-93 See Surveys and Abstracts 1939, p. 224.

ARTHRITIS: I.—ACUTE ARTHRITIS

See also Surveys and Abstracts 1939, p. 226.

ACUTE INFECTIVE ARTHRITIS

Suppurative

94 Treatment with sulphanilamide or sulphapyridine (M & B 693) should be tried in all cases of streptococcal arthritis.

GONOCOCCAL ARTHRITIS

Diagnosis

95 Warren, Hinton, and Bauer found that about 80 per cent of proved cases of gonococcal arthritis gave a positive complement-fixation reaction, and that this was negative in about 20 per cent. Nearly 10 per cent of cases of non-gonococcal arthritis may show a positive gonococcal complement-fixation reaction. A negative reaction therefore does not exclude a gonococcal origin, and a positive reaction in the absence of other evidence of gonococcal infection should not lead to a diagnosis of gonococcal arthritis.

Treatment

Sulphanilamide or sulphapyridine (M & B 693) should be given to all cases. Batchelor *et al.* and Marinkowitch reported favourably on the use of these drugs in gonococcal infections. Keefer and Rantz described in detail the results of treatment in 14 cases of gonococcal arthritis with sulphanilamide. They found that this drug inhibited the growth of gonococci both *in vivo* and *in vitro*, and advocated its use for all cases. They found that it was necessary to maintain a concentration of the drug in the circulating blood of at least 5 mg. per 100 c.cm., to achieve which 4 or 5 grams (60 to 75 grains) must be given daily in divided doses. The drug diffused into the synovial fluid and there reached a concentration equal to that in the blood; in one case the concentration in the synovial fluid was 3 times that in the blood. The synovial fluid became sterile after 3 to 7 days of treatment. On withdrawal of the drug there may be a recrudescence of arthritis or neuritis. The authors emphasize that all side-effects of the sulphanilamide treatment should be carefully watched. In their series 4 patients showed these effects, namely, in 1, haemolytic anaemia, in 1, fever, and in 2, febrile reaction with a rash. All the patients showed mild symptoms during treatment, e.g. cyanosis, and feelings of depression and weakness.

Artificial fever. A report by Krusen and Elkins on fever therapy by physical means, authorized by the Council on Physical Therapy of the American Medical Association, confirms the use of physically-induced artificial fever in the treatment of gonococcal arthritis. Under this treatment 60 to 80 per cent of the patients are freed from their symptoms, and an additional 10 per cent are improved. The method of treatment is the same as that for other forms of gonorrhoea—namely one session lasting 10 hours, during which the body temperature is maintained at 106 to 107° F. (41·1 to 41·6° C.). The treatment is more effective in early than in late cases.

PNEUMOCOCCAL ARTHRITIS

96 Treatment with sulphapyridine (M & B 693) should be tried.

MENINGOCOCCAL ARTHRITIS

97 The first and second types described should receive treatment with sulphanilamide or sulphapyridine (M & B 693). It is important to note that benzylsulphanilamide (proseptasine) was of very little, if any, value in meningococcal infection.

Batchelor, R. C. L., Lees, R., Murrell, M., and Braine, G. I. H. (1938) *Brit. med. J.*, **2**, 1142.
Keefer, C. S., and Rantz, L. A. (1939) *Amer. J. med. Sci.*, **197**, 168.
Krusen, F. H., and Elkins, E. C. (1939) *J. Amer. med. Ass.*, **112**, 1689.

Marinkowitch, R. (1939) *Brit med J*, 1, 317.
Warren, C F., Hinton, W. A., and Bauer, W (1937) *J Amer med Ass.*, 108, 1241.

97

ARTHRITIS: II.—RHEUMATOID ARTHRITIS

See also Surveys and Abstracts 1939, p 226

TREATMENT

Orthopaedic Measures

98

A very successful method of 'serial plasters', which was a compromise between rest and movement, was recently introduced The aim was to check the tendency to contracture, present in the joints of so many active cases, and at the same time to allow the inflammatory swelling around these joints to subside and disperse. The affected joints were put into a light plaster of Paris cast, in the best position obtainable In some cases a brief anaesthetic such as evipan may be used with this object, but the joint should not be forced much beyond what it can achieve when the patient is conscious After an interval which should not exceed a week, this cast must be bivalved and the joint gently put through full movement In nearly every case the short period of immobility will have reduced the swelling and, muscle spasm having also been relieved, the limb will be straighter and capable of freer movement than previously This process may be repeated several times until the affected limb appears to be straight When this has been done, the lower half of the last cast should be kept and used as a splint which the patient should sleep in for a month or two and also wear during periods of the day if any tendency to contracture again occurs That no unsplit cast is left on a limb for more than a week is an efficient safeguard against the occurrence of any ankylosis

ARTHRITIS: III. MENOPAUSAL ARTHRITIS

AETIOLOGY AND TREATMENT

99

In discussing the existence of menopausal arthritis as a clinical entity, Hall divided patients with joint disturbances during the menopausal period into 2 groups (i) In some there is evidence of thyroid deficiency the association of these conditions also occurred in men and in younger patients (ii) In others without evidence of thyroid deficiency, deficiency of ovarian secretion was regarded as an important causal factor In 71 women with arthralgia or arthritic symptoms after removal or destruction of the ovaries many of whom were treated with oestrogenic hormone, striking benefit followed 53 of the patients were diagnosed as arthralgia and 18 as true arthritis atrophic (rheumatoid) hypertrophic (osteoarthritic) and mixed types To 40 of the 53 arthralgic patients oestrogenic hormones in sufficient dosage to control the menopausal symptoms were given in 30 of these the arthralgic symptoms were entirely or practically relieved and in 5 others they were much improved Of the 18 arthritic patients, in 50 per cent the menopausal symptoms and the arthralgia were relieved, and in some cases the arthritis improved For the arthralgic patients progynon B, the benzoic acid ester of oestradiol dissolved in sesame oil was given intramuscularly In some cases progynon D H tablets were given orally but the intramuscular route was preferable Failure of the earlier attempts at oestrogenic therapy was ascribed to inadequate dosage, it was found that larger amounts were usually required to control the arthralgia than to relieve the other menopausal symptoms The usual dosage was 10 000 international units twice a week for 4 to 6 weeks Symptoms did not generally improve until the third week of treatment In some cases 5 times this amount seemed a more adequate dose

Hall, F C (1938) *New Engl J Med*, 219, 1015

ARTHRITIS: IV.—OSTEOARTHRITIS

See also Surveys and Abstracts 1939, p 228

AETIOLOGY

Incidence, Distribution, and Predisposing Causes

'*Degenerative Arthritis*'

100

Bauer and Bennett have shown that degeneration of the articular cartilage normally begins much earlier in life than was hitherto supposed, namely from the third

100 decade onwards. Many factors might expedite this ageing process in the articular cartilage. Inheritance of a particular type of cartilage probably played a part, but Bauer and Bennett laid even greater stress upon the traumatic factor. An isolated injury might start the train of changes or, on the other hand, a series of injuries or contusions, such as might be associated with certain occupations, appeared to be an important cause of early degenerative changes.

Accelerating Factors in Chronic Hypertrophic Arthritis

Haden and Warren, in an investigation of 50 osteoarthritic patients, attempted to show that degeneration of the articular cartilage was expedited by a lowered metabolic rate, obesity, endocrine disorders, and disturbances of the circulation.

TREATMENT

Osteoarthritis of the Hip-Joint

McMurray strongly recommended subtrochanteric bifurcation osteotomy of the hip-joint (Lorenz) for arthritis associated with severe pain, and described his results. This operation, however, had the drawback associated with some other operations upon the osteoarthritic hip, such as arthrodesis, necessitating a lengthy post-operative immobilization in plaster.

Smith-Petersen considered that the pain in osteoarthritis of the hip was due to the prominent anterior lip of the acetabulum impinging upon the neck of the femur, and therefore advised operative removal of the anterior margin of the acetabulum, and claimed satisfactory results. He also, however, recommended removal of part of the anterior portion of the capsule of the hip-joint; probably much of the benefit after the operation was due to this procedure. More recently satisfactory results have been claimed from such a removal of capsule only, and this method is worthy of, and will doubtless be subjected to, further trial. Tumbrell Fisher has for many years held that the pain of an osteoarthritic joint was due more to changes in the capsule and synovial membrane than to the actual approximation of articular surfaces, and proposes to investigate the possibility that capsulectomy combined with manipulation in a series of cases will be successful

Smith-Petersen also described a method of preventing restiffening of the hip-joint after arthroplasty by covering the reshaped femoral head with a mould composed either of glass (pyrex), bakelite, or vitallium. In his first case the mould was removed at a subsequent operation, but subsequently he obtained good results by leaving the vitallium mould *in situ*. The operation is at present in the experimental stage, but constituted a bold attempt to overcome the restiffening so frequent after arthroplasty of the hip.

Bauer, W., and Bennett, G. A. (1936) *J. Bone Jt Surg.*, **18**, 1
Haden, R. L., and Warren, W. A. (1936) *J. Lab. clin. Med.*, **21**, 448.
McMurray, T. P. (1935) *Brit. J. Surg.*, **22**, 716
Smith-Petersen, M. N. (1936) *J. Bone Jt Surg.*, **18**, 869
(1939) *ibid.*, **21**, 269

ARTHRITIS: VI.—ARTHRITIS IN CHILDREN, OR STILL'S DISEASE

See also Surveys and Abstracts 1939, p. 230

TREATMENT

102 At the International Congress on Rheumatism and Hydrology held in 1938, a discussion was devoted to the treatment of juvenile rheumatism. B. de Horvath classified the treatment as follows: chemotherapy, which had gained much from the use of gold preparations, though these must be used with great caution; ray therapy; balneotherapy, and mechanotherapy, which aimed at the prevention or cure of contracture of muscles and deformities of joints. He also commented on the fact that the incidence of juvenile rheumatism in Hungary, which was formerly about half that in Western European countries, appeared from the last published statistics to have increased fivefold.

J. Forestier, F. Françon, and J. Herbert reported the orthopaedic treatment of pronounced deformities of the legs of a boy, aged 11, who had been confined to bed for 2 years with the hips and knees flexed and immobilized by muscular con-

tracture. Plaster was applied to both legs and to the trunk as far forward as the ribs, with the greatest degree of extension that was painless. After 12 to 17 days the plaster was bivalved, the posterior part only being retained. Active and passive movements and massage were instituted. During 8 months 6 plasters were applied: with each the contracture diminished and extension increased. Fibrous adhesions were then broken down by extension under anaesthesia and a plaster was applied for 42 days. It was considered that this method of the Boston School also caused improvement in the patient's general condition. 102

G. Edström reported on the favourable results obtained with gold salts at the clinic of the University of Lund. It was considered that the disadvantages of this treatment were more than balanced by the advantages, and, in fact, that signs of intolerance often synchronized with the improvement in the clinical picture, as if the curative dose almost coincided with the maximal tolerated dose. Stress was laid on the need for caution in the use of the drug, and its restriction to chronic cases. At Lund solganal B oleosum intramuscularly was the usual routine, but sometimes solganal intravenously was used. Edström also emphasized the beneficial results of blood transfusion in debilitated cases: 400 to 500 c.cm. at monthly intervals was insisted on. Plaster of Paris was also recommended for the prevention and correction of contractures and deformities- either plaster bandages or splints. Fixation in plaster must not be continued longer than 5 to 7 days, after which a splint should be applied which allows the joints to be carefully moved, actively if possible, at least once each day.

Proceedings of the International Congress on Rheumatism and Hydrology (London and Oxford) and the Bicentenary Congress on Chronic Rheumatism (Bath) (1938) London, pp. 158, 168, 170

ASCARIASIS

See Surveys and Abstracts 1939, p. 230. 105

ASCITES

See Surveys and Abstracts 1939, p. 230. 106

ASPHYXIA IN CHILDREN

See Surveys and Abstracts 1939, p. 231. 109

ASTHMA

See also Surveys and Abstracts, p. 231

TREATMENT

Prevention of Attacks

In a review of the dietetic treatment of asthma Bray stated that, apart from specific sensitivity, distension of the stomach by large meals or the production of gas might irritate the vagus and excite asthmatic symptoms; that hypochlorhydria might lead to absorption of imperfectly digested proteins with allergic properties; that food sensitivity might be associated with other types of sensitivity and aggravate the symptoms; that apparent discrepancies between skin tests and the occurrence of symptoms might be due to changes produced in the food by cooking or digestion, by admixture with other foods, by factors such as fatigue, illness, changes in the nervous or mental state or in the basal metabolic rate, and by cyclical changes in susceptibility. The diet must finally be settled by trial and error. 110

Bray, G. W. (1938) *Practitioner*, **141**, 97.

ATAXY

See Surveys and Abstracts, p. 234. 112

ATHLETICS AND ATHLETIC INJURIES

See also Surveys and Abstracts 1939, p. 235.

ATHLETIC INJURIES

Treatment of Sprains and Painful Joints

115 Ethyl chloride spray is in common use as a local anaesthetic in minor surgery. Its value for this purpose is doubtful; at the most it appears to deaden sensation. Recently this property has been used in minor orthopaedic cases to relieve muscle spasm and to numb sensitive areas sufficiently to enable simple manipulative treatment to be carried out; for example, in tennis elbow it is often difficult to obtain full extension of the elbow-joint because of spasm of the biceps, the taut tendon being very obvious in the antecubital fossa. If the area over the antecubital fossa and the common extensor origin is sprayed with ethyl chloride until 'frost' just begins to appear, it will be found that the spasm is inhibited for several minutes, during which time the joint can be put through a full range of movements. The increased range and absence of pain are very striking, and often make it possible to break down adhesions without discomfort. The advantage of being able to deal with small joints without a general anaesthetic is obvious, and the method deserves to be more widely known.

Recent articles have emphasized the therapeutic value of injections of local anaesthetics and of physiological saline in acute and chronic sprains. In acute sprains a tender point often corresponds with the torn fibres of some ligamentous structure, for example, below the external malleolus in sprains of the external lateral ligament of the ankle. Much of the immediate disability is due to reflex muscular spasm, and the injection of 2 to 3 c.cm. of 1 per cent novocain (procaine hydrochloride) at the site of tenderness is often followed by striking relief for several hours. If this is supplemented by adequate physical treatment in the form of ionization, massage, and faradic muscular contractions, all designed to promote absorption of exudate, the period of disability can be materially shortened.

In chronic cases organization of the exudations produces firm fibrotic areas in the tissues near the site of the injury. This fibrositis is often very resistant to treatment, and is responsible for much of the minor pain and discomfort described as muscular rheumatism. The injection of 5 to 10 c.cm. of sterile physiological saline in conjunction with proper physical treatment produces striking results in many cases. The saline is injected into the substance of the fibrous mass, and its action is probably largely mechanical, breaking up the fibrotic masses and provoking reaction. The injection is painful and should be preceded by the injection of 2 to 3 c.cm. of local anaesthetic. In successful cases there is often a slight febrile reaction 6 to 8 hours after the injection.

AVIATION (MEDICAL EXAMINATION OF PILOTS)

See also Surveys and Abstracts 1939, p. 236.

GENERAL

116 Advances in design and performance of aircraft throw increasing strain on the human element, necessitating alteration of standards and tests. A Flying Personnel Research Committee has been formed by the British Government to investigate especially problems of vision, improvement of oxygen supply (in view of stratosphere flying), and increase of man's endurance both as regards altitude and range of flight.

The effects of 'blacking-out', fatigue, and strain, the ill-effects of sound, and the problem of pre-selection of candidates are also special problems under review.

BACKACHE AND LUMBAGO

117 See Surveys and Abstracts 1939, p. 238.

BALANITIS

119 See Surveys and Abstracts 1939, p. 155.

BARTONELLOSIS

VERRUCA PERUVIANA (LOCALIZED BARTONELLOSIS)

Treatment

Manrique has reported upon the results of 12 cases treated with the aromatic arsenic and antimony preparation 386 B. The drug was injected intravenously in doses of 0·1 to 0·3 g. and, when repeated 2 or 3 times, banished the *Bartonella* from the blood stream and brought about a rise in the blood count. A total of 5 to 7 g. has been injected without provoking any untoward symptoms. The reports concerning the verruca stage, as far as they go, are also distinctly favourable. 122

Manrique. Quoted by Kikuth, W. (1937), *Arch. Schiffs- u. Tropenhyg.*, **41**, 729.

BELL'S PARALYSIS

See also Surveys and Abstracts for 1939, p. 88.

Discussing the aetiology of facial paralysis, Critchley emphasized the possibility that some cases of Bell's paralysis might be the result of infection with a neurotropic virus. Cawthorne described the possible methods of operation, namely relief of compression or, in traumatic cases when division of the nerve was suspected, restoration of continuity by apposition of the divided ends or by bridging the gap by a homogeneous nerve graft. He stated that absence of galvanic response in the facial muscles, indicating replacement of muscle by fibrous tissue, indicated that operation was useless 124

Cawthorne, T. (1937) *Trans. med. Soc. Lond.*, **60**, 171
Critchley, M. (1937) *Trans. med. Soc. Lond.*, **60**, 166. Reported also in *Lancet* (1937), **1**, 390

BERI-BERI

See also Surveys and Abstracts for 1939, p. 239.

AETIOLOGY AND PATHOLOGY

Vitamin B_1

In 1937 the successful synthesis of vitamin B_1 was reported in America by Cline, Williams, and Finkelstein, in England by Todd and Bergel, and in Germany by Andersag and Westphal; and the pure substance is now available commercially. Its chemical properties are described in Vol. XII, on p. 578 125

The substance is unique in that it is the only known naturally occurring compound containing the thiazole nucleus. A pyrophosphoric ester of vitamin B_1 has been isolated from yeast, and there is some evidence that in certain instances conversion into the pyrophosphate precedes the utilization of the vitamin, although on injection into avitaminous animals the pyrophosphate acts more slowly than the vitamin itself. This may, however, be due to adsorption of the ester by the tissue proteins retarding diffusion, since the two compounds act with equal speed when given by the mouth.

The vitamin is present in practically all natural animal and vegetable tissues used as food, but the amount is usually small, being of the order of one part per million. White flour, milled rice, macaroni, spaghetti, white breakfast cereals, and cane sugar contain only negligible amounts. The richer sources are whole seeds, pork, milk, liver, heart, and kidney. An important loss occurs in the decortication of grain, and, as there are no compensatory superlatively rich sources among the more commonly employed foodstuffs, it is probable that, under modern conditions, some degree of vitamin B_1 deficiency is extremely wide-spread.

Most observers believe that little destruction of vitamin B_1 occurs in foodstuffs exposed to 100° C., but undue heat is undesirable and, as the vitamin is sensitive to alkalis, the addition of cooking soda to vegetables should be avoided. It is to some extent adsorbed on the starches, but it may be lost by solution in cooking;

125 therefore cooking water and juices should not be discarded but should be incorporated into soups, sauces, or gravies.

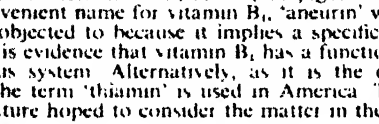
The average daily requirement for man is about 1 to 2 mg., although to some extent it is dependent on the physical work performed and the amount and type of food consumed, a rough guide being that the ratio of vitamin B_1 to non-fat Calories should not be less than 1/3000. The body does not appear to store an appreciable amount of vitamin B_1, and a daily intake of 0·75 mg. probably represents a 'borderline' supply; with such an intake excessive work, infection, or increased metabolism may precipitate the development of frank symptoms. The amount present in human blood appears to vary in disease, but in the normal person is about 0·008 mg. per 100 c.cm. of blood.

Vitamin B_1 is sometimes expressed in terms of various units, but different laboratories are not always in agreement even upon the values of these units, and now that the pure product is available it seems desirable to express all values in terms of weight of pure crystalline vitamin B_1; the approximate value for the more commonly employed unit is that 1 g. of vitamin B_1 is equivalent to 300,000 international units, 600,000 Sherman units, or 400,000 pigeon units.

As a convenient name for vitamin B_1, 'aneurin' was suggested by Jansen, but this has been objected to because it implies a specific connexion with nerve function, and there is evidence that vitamin B_1 has a function even in organisms which have no nervous system. Alternatively, as it is the only known vitamin containing sulphur, the term 'thiamin' is used in America. The International Committee on Nomenclature hoped to consider the matter in the autumn of 1939.

Physiology

Experiments on the respiration of brain tissue *in vitro* show that vitamin B_1, or its pyrophosphate, is concerned with the removal by oxidation or otherwise of an intermediary product of carbohydrate metabolism, probably pyruvic acid, as indicated simply in the following diagram



It has also been suggested that, in the presence of vitamin B_1, pyruvic acid may serve as an intermediary in the synthesis of fat. Williams has pointed out that vitamin B_1 is universally distributed in living tissue, and that deficiency affects every tissue, he says 'carbohydrate metabolism cannot go forward in any living cell without thiamin (vitamin B_1)'.

Excess of pyruvate can be demonstrated in the blood in beri-beri, but this is only an expression of the disordered metabolism, since there is no evidence that injections of pyruvic acid are themselves toxic (Peters). The normal value for man's blood is between 0·4 and 0·6 mg. per 100 c.cm. of blood, the cerebrospinal fluid containing about half this amount, but, in fulminating beri-beri, values of over 1 mg. and even as high as 6 or 7 mg. per 100 c.cm. of blood have been recorded. When no complicating factor is present these high values may be restored to normal in 10 to 15 hours after the administration of 5 mg. of vitamin B_1. Following muscular exercise a rise of blood pyruvate may be shown in the healthy person, but this rapidly returns to normal. In addition to the experiments with brain tissue it has been shown that the reduced oxygen-uptake of kidney tissue from avitaminous pigeons can be restored to normal by vitamin B_1, this is of interest in relation to the oedema of beri-beri, and it may be pointed out that avitaminous pigeons are in a state of latent oedema which can be made manifest by giving them salt. It has also been claimed, but not so clearly established, that vitamin B_1 exerts a similar effect upon the respiration of heart muscle.

In experimental animals the first effect of deprivation of vitamin B_1 is loss of appetite, which is perhaps secondary to failure of cellular nutrition. This is naturally followed by loss in weight, and when about one-third of the original weight has been lost the characteristic nervous signs become apparent. This is usually referred to as a 'polyneuritis', but, as the process is a dysfunction and non-inflammatory, the term 'neuropathy' is perhaps better. Changes in temperature, loss of vision, bradycardia, and a decreased sugar tolerance may be found, and are usually attributed

to functional derangements in various centres of the brain Minz, discussing the functional liberation of acetylcholine by the vagus, states that the action of acetylcholine is reinforced by the presence of vitamin B_1, and suggests that this may help to interpret the syndrome of vitamin B_1 deficiency Oedema may sometimes occur The syndrome rapidly clears up on administering vitamin B_1, so that it is a manifestation of a functional failure, rather than of an irreversible structural change

In man the nervous phenomena are comparable to those of experimental animals The neuropathy is wide-spread, involving not only the central nervous system and the peripheral nerves but also the sympathetic ganglia (Vedder) The circulatory disturbances include, singly or in combination, right ventricular failure peripheral arteriolar dilatation, peripheral circulatory collapse, and shock (Weiss and Wilkins, 1936 and 1937) This may be partly due to dysfunction of the vagus but is generally considered to be due mainly to hydropic degeneration of the myocardium It is also possible that the changes in the sympathetic ganglia may lead to disorders of the peripheral circulation In beri-beri the heart-rate is usually accelerated, although less so than in many acute toxic conditions, and in hunger oedema definite bradycardia may be found This is of interest in view of the bradycardia which appears specifically to follow vitamin B_1 deficiency in animals, although Parade and Sampson have each pointed out that simple inanition and increasing age also lead to bradycardia in animals

A number of explanations have been advanced to explain the oedema of beri-beri It may be dependent on a specific effect of vitamin B_1, in the absence of which an intracellular oedema occurs, in some cases it results from cardiac failure or an increase in capillary pressure in others it seems associated with a fall in the plasma proteins and, finally, a functional failure of renal secretion, in turn influenced by the general cardiovascular derangement, may play some part The association of muscular exercise is interesting, if the patient is disabled by the neuropathy, oedema is unlikely to develop, but, if muscular work is still possible, cardiac insufficiency and oedema will probably result (Keefer)

CLINICAL PICTURE

Classification of Types

Ordinary Beri-Beri

Cardiac symptoms Dustin, Weyler and Roberts report the following electrocardiographic changes in alcoholic patients presenting cardiovascular symptoms of dyspnoea, oedema and tachycardia associated with vitamin B_1 deficiency The tracings showed low voltage flattening of the T wave increase in the Q-T interval, and moderate sinus tachycardia In Leads I and II some cases showed inversion of the T wave, even suggesting cardiac infarction, excepting that the change in the apical chest lead was less than in the limb leads, and deviations of the RS-T segment were slight or absent The condition improved with rest, balanced diet, and 10 mg. of vitamin B_1 daily

Acute Fulminating Beri-Beri

Murakoshi, Hashimoto, Strauss, Hawes and others have described the dramatic effect of vitamin B_1 in acute fulminating beri-beri In such cases the patients are breathless, restless, and vomiting the veins are engorged, there are cardiac dilatation, particularly right-sided, and moderate tachycardia the diastolic pressure is invariably low, the pulse may be imperceptible and, without treatment, death occurs within a few hours These moribund patients, after receiving an adequate amount, 5 mg or more, of pure vitamin B_1 intravenously, become less restless often within a few moments, after an hour or so the diastolic pressure begins to rise and the patient may even be able to get out of bed, within a few days the pulse rate slows, diuresis occurs, oedema lessens, and the patient is incredibly improved The vitamin must be given in adequate amounts, and injected intravenously to have any rapid effect, the reaction is quantitative, and, if insufficient vitamin is given, temporary amelioration may occur, but be followed by a sudden return of dyspnoea or collapse and death The vitamin appears to be non-toxic and, although in these acute cases the systolic pressure rises with the diastolic, and the arteries feel increasingly rigid, the heart does not appear to labour After a week this condition returns to normal while, in normal persons and in cases of hypertension and chronic renal disease, no effect on blood pressure has been observed In acute beri-beri the kidney frequently shows a functional insufficiency giving rise to scanty urine with albumin and casts, and a high blood urea which falls as the urine increases after treatment

Infantile Beri-Beri

According to Chan the common symptoms of beri-beri in infants are vomiting, sometimes severe, aphonia which is most striking, oedema mainly of the face and extremities and, in about 75 per cent of cases, loss of knee jerks; more than 50 per cent of the cases show symptoms between the third and fourth weeks of life. More than half the mothers had signs of beri-beri, and in most instances there was a history of previous babies having died of a similar condition. With treatment consisting of replacing breast-feeding by the administration of vitamin B_1 extracts, the vomiting was the first symptom to disappear, and the aphonia the last.

Pellagroid Beri-Beri

There is a possibility that inadequate diets may be deficient in more than one factor, and several cases of the pellagroid beri-beri syndrome have been recorded. In such cases skin and mucous membrane lesions have been cured with nicotinic acid, but the neuritic symptoms only disappeared when vitamin B_1 was introduced. Spies and Aring express the reasonable view that there is no difference between the neuritis of beri-beri and that of pellagra.

Other Types

There is evidence that vitamin B_1 is necessary for the metabolism of alcohol in the body, as it is for carbohydrate, and an increased intake of alcohol requires an increased intake of vitamin B_1. Alcoholic beverages, however, are practically devoid of vitamin B_1 and, furthermore, in chronic alcoholism, appetite becomes lost, other foodstuffs are replaced by alcohol, and absorption of the vitamin may also be impaired by an alcoholic gastro-enteritis. There is now considerable evidence that so-called alcoholic neuritis is in fact due to vitamin B_1 deficiency, and can be prevented or cured by administration of vitamin B_1.

Some abnormal state of the intestinal canal may also lead to defective absorption of vitamin B_1, even though there is no actual deficiency in the diet, although the condition is often exaggerated by a restricted dietetic regime. A relative vitamin deficiency may also arise from increased demands such as may occur in pregnancy, diabetes mellitus, febrile states, or conditions of increased metabolism.

Surgery in Beri-Beri

Pflomm has drawn attention to the fact that natives in South China stand abdominal operations badly. He believes one of the causes to be beri-beri, and, as the condition is wide-spread and may give little evidence of its imminence, he treated all his operation cases with cardiac tonics. Now that pure vitamin B_1 is available adequate supplies might be given to surgical cases in which beri-beri is a likely complication.

DIAGNOSIS

Meyers employs two clinical tests for beri-beri. The first is the development of a sound, audible with a stethoscope over the cubital fossa, following an injection of adrenaline. Sometimes in pronounced beri-beri such sounds are already audible over the large vessels before the injection of adrenaline but in these cases the injection emphasizes them.

The second and more important test depends on the diuresis following drinking 1 litre of water by the fasting patient. The diuresis is recorded half-hourly for 4 hours, by which time all the ingested water will have been excreted by a normal person, due allowance being made for sweating. In beri-beri, not only is there delayed excretion but, what is more significant, the excretion is restored to normal by administration of vitamin B_1 (Volhard's diuresis test).

TREATMENT

Prophylaxis

Toullec has pointed out that it is sometimes difficult to persuade the native to use unpolished rice as he objects to its taste, and will say that it does not satisfy his hunger. It is suggested therefore that rice be decorticated in such a way that the vitamin B_1 is retained, as in 'parboiling' or by milling so that only the bran is removed and the embryo left. Other successful measures employed, for example by the Government of the Netherlands Indies, consist of encouraging the growing and consumption of leguminous plants, the distribution of half-polished rice, and the strict control of the diet of estate labourers.

Curative Treatment 125

The remarkable effects of vitamin B_1 in acute cardiac beri-beri have already been discussed. Now that the pure vitamin is available, further studies of its therapeutic value in less clearly defined syndromes will be awaited with interest, particularly as there is good reason to believe that the vitamin B_1 intake of very large numbers of persons under modern conditions is relatively deficient.

Andersag, H., and Westphal, K. (1937) *Ber. dtsch. chem. Ges.*, **70**, 2035.
Chan, M. (1935) *Chin. med. J.*, **49**, 676.
Cline, J. K., Williams, R. R., and Finkelstein, J. (1937) *J. Amer. chem. Soc.*, **59**, 1052.
Dustin, C. C., Weyler, H., and Roberts, C. P. (1939) *New Engl. J. Med.*, **220**, 15.
Hashimoto, H. (1937) *Amer. Heart J.*, **13**, 580.
Hawes, R. B. (1938) *Trans. R. Soc. trop. Med. Hyg.*, **31**, 475.
Keefer, C. S. (1930) *Arch. intern. Med.*, **45**, 1.
Meyers, F. M. (1938) *Geneesk. Tijdschr. Ned.-Ind.*, **78**, 1537.
Minz, B. (1938) *Pr. méd.*, **46**, 1406.
Murakoshi, Y. (1936) *Bull. nav. med. Ass., Japan* (Abstr. Sect.), **25**, 62.
Parade, G. W. (1937) *Z. Vitaminforsch.*, **6**, 327.
Peters, R. A. (1938) *Trans. R. Soc. trop. Med. Hyg.*, **31**, 483.
Pflomm, E. (1935) *Münch. med. Wschr.*, **82**, 661.
Sampson, W. I. Quoted by Williams, R. R., and Spies, T. D.
Spies, T. A., and Aring, C. D. (1938) *J. Amer. med. Ass.*, **110**, 1081.
Strauss, M. B. (1938) *J. Amer. med. Ass.*, **110**, 953.
Todd, A. R., and Bergel, F. (1937) *J. chem. Soc.*, 364.
Toullec (1938) *Rev. méd. franç. d'Extrême-Orient*, **16**, 108.
Vedder, E. B. (1938) *J. Amer. med. Ass.*, **110**, 893.
Wechsler, I. S. (1938) *J. Amer. med. Ass.*, **110**, 1910.
Weiss, S., and Wilkins, R. W. (1936) *Trans. Ass. Amer. Phys.*, **51**, 341.
— (1937) *J. Amer. med. Ass.*, **109**, 786.
Williams, R. R. (1938) *Science*, **87**, 559.
— and Spies, T. D. (1938) *Vitamin B_1 (Thiamin) and its use in Medicine*, New York.

BILHARZIASIS

See Survey and Abstracts 1939, p. 240 126

BIRTH PALSIES

See Surveys and Abstracts 1939, p. 240. 128

BITES AND STINGS

See Surveys and Abstracts 1939, p. 241. 129-134

BLACKWATER FEVER

See also Surveys and Abstracts 1939, p. 242.

DEFINITION

Blackwater fever, as shown by Foy and Kondi (1937, a) and others, is now known to be extremely common in Greece, where it can be studied in hospital by modern methods. Its immediate cause is still unknown, but N. H. Fairley and his colleagues have discovered in blackwater fever a new pigment derived from haemoglobin which provides for the first time a method of distinguishing blackwater fever from haemoglobinuria. A complete summary of the literature regarding this disease, with a full account of treatment, was given by J. W. W. Stephens. 135

MORTALITY AND ECONOMIC IMPORTANCE

Mortality.—A summary of malarial conditions in the Belgian Congo, by Duren, pointed out that in that country, with a total European population of 18,500, in

the years 1918–34 1,115 cases of blackwater fever had been recorded, 217 of which proved fatal, giving a case mortality of 19 per cent, which is a little lower than that (23 to 26) given in Vol. II, p. 362.

AETIOLOGY

Theories of Causation

Practically all observers still note the close association between this disease and antecedent malaria. In confirmation of the view that no special parasite, or even any 'haemolytic' strain of malaria parasite, was concerned, Foy and Kondi recorded that inoculation of 106 mental patients with blood drawn from 58 cases of blackwater fever, at various times after the occurrence of haemoglobinuria, in no case resulted in haemoglobinuria. The result was the same when 68 patients with general paralysis were bitten by mosquitoes previously fed on 35 patients suffering from blackwater fever.

The possibility that deficiency in diet might play some part in causation receives some support from the fact that in Greece its unusual prevalence appeared to be associated with large-scale immigration of refugees from Asia Minor. It had also been suggested that deficiency of vitamin C might be an auxiliary by decreasing the amount of anti-haemolysin. Further, to bring the condition into line with recent ideas on immunity, it had been suggested that in malaria, whereas individuals who react well to small infections of malaria acquire an immunity (see supplementary notes on malaria, p. 129), those who do not react well, or in whom premunition is exhausted or diminished by causes, such as cold, fatigue, and quinine, develop blackwater fever. Concrete evidence in support of all these views, however, is still lacking.

PATHOLOGY

Pathology of Blood and Urine

In addition to oxyhaemoglobin, methaemoglobin in the plasma has been recorded by Yorke (1909) and others, it appears, however, that the pigment taken to be methaemoglobin is an entirely new and hitherto unknown haemoglobin-derivative called by its discoverer pseudo-methaemoglobin. This has been constantly demonstrated in severe blackwater fever, whereas methaemoglobin does not occur in the plasma. The presence of methaemoglobin in the urine is due not to its excretion as such from the plasma, but to alteration of haemoglobin after excretion in the renal tubules or bladder. The new pigment has characteristic spectroscopic appearances and behaviour. It is produced by the action of plasma upon haemoglobin liberated from the red cells, and therefore indicates intravascular haemolysis. This change can be produced *in vitro* and in fact is the body's normal method for the elimination of free circulating haemoglobin. When methaemoglobin is produced in the blood, e.g. by the action of some drugs, it is present in the red cells and not in the plasma.

Fairley's classification of pigments present in the organs and tissues of the body is as follows. (i) Visceral pigments. (*a*) Malarial pigment or haemozoin: does not give the Prussian blue reaction; occurs in cells of the reticulo-endothelial system as brownish-black granules or clumps of black pigment; is present in small quantities in blackwater fever but, apart from malaria, is seen in only one other disease, namely bilharziasis in which it is formed from partly digested blood regurgitated into the area of the portal vein by the worms, is similar to, if not identical with, haem or haematin. (*b*) Haemosiderin: normally a fine brown pigment in the parenchymatous cells of the liver, spleen, and kidneys; is greatly increased in blackwater fever and other diseases characterized by considerable haemolysis. (ii) Plasma pigments. (*a*) Oxyhaemoglobin. (*b*) Pseudo-methaemoglobin. (*c*) Bilirubin: hyperbilirubinaemia is seen in all severe cases of blackwater fever. (iii) Biliary and faecal pigments: formed as a direct result of increase in haemobilirubin. (iv) Urinary pigments. (*a*) Oxyhaemoglobin. (*b*) Methaemoglobin. (*c*) Urobilin. (*d*) Brown pigment found as deposit in blackwater-fever urine and blocking tubules of kidney; generally considered to be acid haematin.

TREATMENT

Drugs. How far atebrin can be considered free from the precipitating effects suspected to be associated with quinine is still *sub judice*, but it is usually thought to be desirable to use atebrin in patients known or suspected to be liable to blackwater fever. Two cases following atebrin were recorded from Greece by Foy and

Kondi (1937, b); in these no parasites were seen, though a thick film was taken at the time. 135

Blood transfusion.—Blood transfusion has been extensively used in Southern Rhodesia. It is especially valuable in toxic polyuria and the relapsing type of case and in post-blackwater-fever asthenia. It is contra-indicated in toxic anuric cases. Transfusion should not be delayed until the patient is moribund, and should be repeated until there is microscopical evidence of regeneration of red cells.

Duren, A. (1937) *Mémoires publiés par l'Institut Royal Colonial belge, Sec. des Sci. nat. méd.*, **5**. Abstracted in *Trop. Dis. Bull.* (1938) **35**, 21.
Fairley, N. H. (1937) *Festschr. Bernhard Nocht zum* 80. *Geburtstag von seinen Freunden und Schülern*, Hamburg, p. 123.
Foy, H., and Kondi, A. (1937, a) *Trans. R. Soc. trop. Med. Hyg.*, **31**, 123.
— — (1937, b) *Ann. trop. Med. Parasit.*, **31**, 99.
Stephens, J. W. W. (1937) *Blackwater fever, A Historical Survey and Summary of Observations made over a Century*, London.

BLADDER DISEASES

See Surveys and Abstracts 1939, p. 242. 136-146

BLINDNESS

See Surveys and Abstracts 1939, pp. 128 and 244. 149-162

BLOOD EXAMINATION

See also Surveys and Abstracts 1939, pp. 52 and 245.

CELLULAR CHANGES

DETERMINATION OF CORPUSCULAR VOLUME

For the determination of corpuscular volume and for other haematological procedures, Wintrobe recommended 4 mg. of potassium oxalate and 6 mg. of ammonium oxalate per 5 c.cm. tube. The tubes were prepared by measuring 0·2 c.cm. of a solution containing 2 per cent potassium oxalate and 3 per cent ammonium oxalate into the 5 c.cm. tube, and evaporating to dryness in an incubator. Waxed corks or rubber bungs were essential in order to prevent absorption of plasma. 163

RELATIONS BETWEEN RED-CELL COUNT, HAEMOGLOBIN CONTENT, AND RED-CELL SIZE

Mean corpuscular average thickness.—In certain morbid conditions the normal relation between the volume, the diameter, and the thickness of the red corpuscle is altered. In obstructive jaundice the diameter increases at the expense of the thickness, so that the cell becomes flatter than normal, whereas in acholuric jaundice, particularly the congenital type, the reverse takes place and the cell becomes more globular (spherocytosis). The phenomenon of spherocytosis is detected by correlating the mean corpuscular volume (see Vol. II, p. 474) with the mean corpuscular diameter (see Vol. II, p. 479) and calculating the mean corpuscular average thickness. This is accomplished by assuming that the red corpuscle has the form of a cylinder of known volume and known diameter, from which the height (thickness) can be calculated. The formula for calculation is as follows:

$$\text{Mean corpuscular average thickness in microns} \quad \frac{\text{Mean corpuscular volume}}{\pi\left(\frac{\text{Mean corpuscular diameter}}{2}\right)^2}$$

The normal range is from 1·7 to 2·5μ.

The relation between diameter and thickness can better be appreciated by the diameter-thickness ratio, which is normally 2·4 to 4·2 : 1. Ratios lower than 2·4 indicate spherocytosis.

EXAMINATION OF BONE-MARROW

In certain anaemic states the peripheral blood may not show diagnostic changes and a proper opinion cannot be given without an examination of the bone-marrow.

163 **The procedure is not required as a routine, but is often essential in aleukaemic leukaemia (see Vol. VIII, p. 36), aplastic anaemia, carcinomatosis of bones, myeloma, myelosclerosis, and achrestic anaemia. Bone-marrow examination is also useful for the diagnosis of latent forms of malaria and kala-azar, in which field it has largely replaced splenic puncture. The sternum is the most convenient bone. The marrow may be obtained by needle puncture, the material then being examined as a smear, or with a small 1 c.cm. trephine, the specimen being fixed and examined as a histological section. Sections are essential for the diagnosis of myelosclerosis and usually for aplastic anaemia.**

The technique of sternal puncture is as follows: One hour before operation the patient should receive aspirin, 10 grains, and nepenthe, 15 minims. With the patient lying on his back, the skin, subcutaneous tissues, and periosteum over the sternum, at the level of the second interspace, are infiltrated with a small quantity of 2 per cent procaine hydrochloride (novocain). A Salah needle, previously sterilized in hot oil, is pushed through the skin to the bone, the stop being set at ¼ to ½ inch above the skin level. The needle is then driven through the outer table of the sternum by sharp taps from a small hammer, a definite 'give' is felt as the needle enters the marrow cavity. The stylet is removed and a dry 1 c.cm. syringe attached, and gentle suction applied, a characteristic suction pain occurs if the needle is in the proper place. 0·25 c.cm. of marrow fluid is withdrawn and mixed in a tube with oxalate mixture. No more than this amount should be aspirated because removal of larger quantities causes severe pain. The oxalate mixture is the residue from evaporation in an incubator of 0·1 c.cm. of a solution containing 0·2 per cent potassium oxalate and 0·3 per cent ammonium oxalate. Smears are made from the oxalated fluid within half an hour of collection. A total nucleated-cell count is carried out in a counting chamber, diluting with leucocyte fluid in a red-cell pipette at 1 in 200, or in a leucocyte pipette at 1 in 20, according to the number of cells. Films are stained with Leishman's stain, and a differential count of 400 cells is made.

COAGULATION (BLOOD PLATELETS)

164 In the normal person the platelets in circulation number from 250,000 to 500,000 per c.mm., but there are rapidly alternating periods when platelets are found in large numbers and when they are scanty. It is generally acknowledged that platelets are concerned with three processes, namely coagulation, clot retraction, and adherence to the wall of a damaged blood-vessel for the purpose of temporary repair.

With regard to coagulation, platelets are an important source of thrombokinase or cephaline which, in conjunction with free calcium-ions, activates prothrombin to form thrombin which then interacts with fibrinogen to form fibrin. Comparatively small numbers of platelets will bring about coagulation and another source of thrombokinase, namely damaged tissue cells, contributes to clot formation. The characteristic feature of platelet deficiency is not therefore a prolongation of coagulation time, the result of deficiency is more clearly shown by an interference with the other two functions of platelets. Thus the clot formed is soft and friable for it lacks the presence of sufficient platelets which ordinarily form nodal points for strengthening the fibrin network, the bleeding time is prolonged because it takes time for a sufficient number of platelets to adhere to the damaged vessel-wall and stop the leak. There is also a great tendency to capillary haemorrhage, either spontaneous or as the result of slight trauma, or from pressure such as is applied in Hess's capillary-resistance test.

As a general rule spontaneous capillary haemorrhage does not occur until the platelet count is below the critical level of 40,000 per c.mm. With the possible exception of essential thrombocytopenic purpura haemorrhagica, it is generally acknowledged that mere lack of platelets is not in itself sufficient to account for the occurrence of purpura. There is usually some additional factor which causes damage to the capillary endothelium. This additional factor may be an inherently defective capillary wall or an endothelium damaged by bacterial or virus toxins, poisonous drugs, under-nutrition, or lack of a specific factor—e.g. vitamin C. In practice endothelial damage is a much more common cause of purpura than is a deficiency of platelets. Essential thrombocytopenic purpura haemorrhagica is almost the only haemorrhagic disease in which a reduction in platelets is constant and consistent.

From the opposite aspect it is considered that an excess of platelets implies a

liability to thrombosis. Operative procedures, particularly splenectomy, lead to a vast increase in circulating platelets, and this undoubtedly contributes to the causation of post-operative thrombosis, but here again the condition of the vascular endothelium is an important determining factor. It has been suggested that in haemophilia the platelets are unduly stable, but it is highly improbable that this is the sole cause of the disease. Tocantins has reviewed the whole subject of the mammalian platelet in health and disease. 164

Bleeding time.— A sphygmomanometer cuff is placed on the arm, and the pressure raised to 40 mm., in order to cut off the venous return; the pronator surface of the forearm is then punctured in three places with a stylet to a depth of 2·5 mm., and the blood absorbed on blotting paper, as in Duke's method (see Vol. II, p. 483); 3 punctures are made in order to obtain an average. The maximal normal bleeding time by this method is 240 seconds, but it rarely exceeds 180 seconds (Ivy, Shapiro, and Melnick).

SEROLOGICAL TESTS

AGGLUTINATION TESTS

Glandular fever (Paul and Bunnell Test).— This diagnostic test for infectious mononucleosis is based on the accidental discovery that blood serum contains heterophil antibodies in the form of an agglutinin for sheep's red-cells. The agglutinin is usually sufficiently strong to be diagnostic by the fourth day of the disease, and it is present in high titre during the active phase. The reaction is apparently specific for glandular fever with the single exception of serum sickness, especially recent serum sickness. The agglutinin differs from the 'cold' agglutinin for sheep's cells, sometimes found in normal blood, in that it is usually active at 37° C. and 5° C. 166

There are several methods of performing the test. Variations are confined mainly to the amount of serum used and to the strength of the suspension of sheep's cells. In all methods it is essential first to inactivate the serum by heating for 20 to 30 minutes at 55° C. and to use sheep's cells that are not less than 24 hours old and not more than 5 days old; the cells must be freshly washed on the day of the test. A saline control must always be included in the test.

The following method is satisfactory: 0·25 c.cm. of serum dilutions from 1 in 5 to 1 in 5,000, in tubes with an internal diameter of about 9 mm., are used. To these dilutions are added 0·1 c.cm. of a 2 per cent suspension of sheep cells in physiological saline prepared from thrice washed cells which, with the last washing, have been packed in the centrifuge tube to occupy a volume of about half their original volume. The final serum dilutions therefore range from 1 in 7 to 1 in 7,168. These are incubated in a water-bath at 37° C. for one hour, and then left at room temperature for one hour; when time permits they are placed in the ice-box overnight and read again in the morning after another hour's incubation at 37° C.

The results are read after shaking until all the sediment is evenly suspended. Three grades of agglutination may be recognized: (i) the reaction may be so intense that all the cells remain in one clump, (ii) there may be numerous clumps easily visible to the naked eye; and (iii) the clumps may be so fine that a hand lens or low-power objective is required to see them. The third type is important as it represents the end-point. The diagnostic titre by this method is about 1 in 200 unless the patient is actually suffering from an acute attack of serum sickness; with serum sickness a titre of 1 in 200 does not long persist after the acute phase has passed.

Further studies have shown that the agglutinin in glandular fever is different from that found in serum sickness and from that sometimes found in low titre in normal serum; whereas the first is adsorbed by ox cells but not by guinea-pig's kidney, the second is adsorbed by both these tissues, and the third is adsorbed in an opposite manner to the first.

Davidsohn described this adsorption technique in detail and emphasized its utility when serum sickness cannot be excluded, as well as for identifying significant low titre reactions such as may be found in late cases.

PHYSICAL AND CHEMICAL CHANGES

SEDIMENTATION OF RED CELLS

Correction of the Sedimentation Rate for Anaemia

When the sedimentation rate is determined by Wintrobe's method (see Vol. II, p. 493) the tube may afterwards be centrifugalized to determine the corpuscular 167

volume. The following chart enables the observed sedimentation rate to be corrected for anaemia, which is estimated by the observed corpuscular-volume.

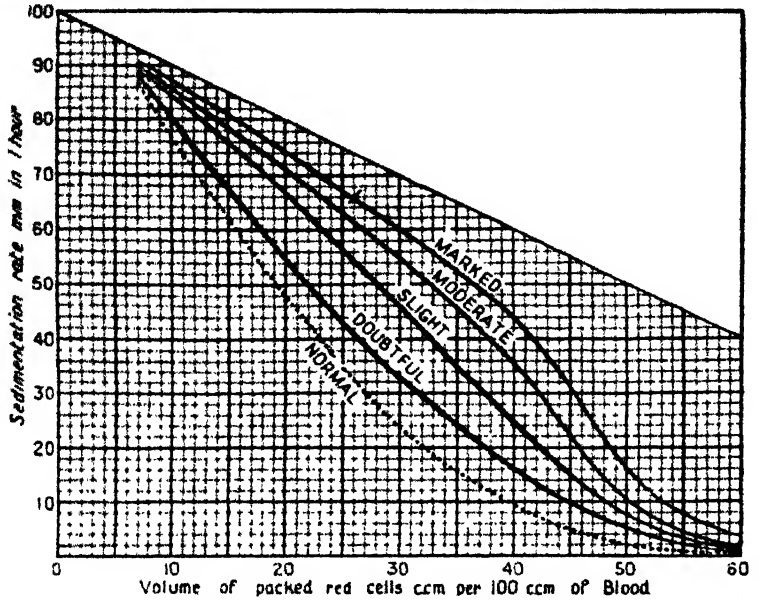


FIG. 3. Chart based on multiple observations to enable sedimentation to be corrected for anaemia. To correct for anaemia, find the junction of the lines for the observed sedimentation rate and the observed corpuscular volume. This will fall in one of the zones (normal, doubtful, etc.) which indicates the degree to which the sedimentation rate is affected.

For example. Observed sedimentation rate 60 mm.; observed corpuscular volume 25 c.cm.; true sedimentation is 'slightly' increased. If an approximate compensated figure is required, follow the nearest curve down to the point where it cuts the 45 c.cm. vertical line (average normal volume of packed red-cells irrespective of sex); the horizontal line at this point is the approximate corrected sedimentation rate. In the example given above, this figure is 19 mm. (From *Lancet*, 1938.)

FRAGILITY OF THE RED CELLS

Quantitative method. Fragility is influenced by a number of physical factors which, for an accurate test, must be eliminated as far as possible. The carbon-dioxide content of the blood has a definite effect, and this may be avoided by fully oxygenating the blood under test. Other sources of error are inaccurate saline solutions, failure to mix properly, and variations in the *p*H of the distilled water used for diluting the saline. This last is minimized by using whole blood at a dilution of 1 in 25 which allows the blood plasma to act as a buffer (Creed). Distilled water should be boiled and stored in bottles with a soda-lime air filter to prevent absorption of carbon dioxide. Anaemia *per se* decreases fragility; an anaemic person may therefore not exhibit minor degrees of fragility until the anaemia is cured (Creed).

Method based on Creed's technique. A stock 25 per cent solution of sodium chloride in distilled water is prepared from the pure salt which has been dried to constant weight by heating and allowing to cool in a desiccator. At the time of the test, 4 c.cm. of this stock solution is diluted with distilled water in a measuring cylinder to 100 c.cm. to make a 1 per cent solution, and mixed thoroughly. The distilled water must be reliable. A series of 12 tubes (3½ × ¾ in.) are set up in a rack. To the various tubes, using a tested dropping pipette, are added the number of drops of distilled water and of 1 per cent sodium chloride solution according to

the following table. This gives a series of saline concentrations ranging from 0·28 per cent to 0·72 per cent with intervals of 0·04 per cent. It is essential to ensure thorough mixing of the saline and distilled water before proceeding to the next step, namely, the addition of one drop of blood to each tube in the series.

Distilled water (drops) –	18	17	16	15	14	13	12	11	10	9	8	7
1 per cent NaCl (drops) –	7	8	9	10	11	12	13	14	15	16	17	18
Concentration NaCl (per cent) –	0·28	0·32	0·36	0·40	0·44	0·48	0·52	0·56	0·60	0·64	0·68	0·72

As to the blood used for the test, Creed collects this from a vein with a dry sterile needle, allowing the blood to run directly into a wide test-tube which has previously been waxed to prevent clotting. Others use heparinized blood, or blood that has been collected into Wintrobe's isotonic ammonium and potassium oxalate mixture (see p 38). The blood must be thoroughly oxygenated, either by blowing a current of air vigorously over the surface by means of a hand bellows with a glass delivery tube drawn out to a wide capillary, or by rolling the blood around in a wide bottle or a large tube. Aeration should be carried out for 4 minutes. After adding the blood, the tubes are inverted to ensure mixing, and this is repeated 10 minutes later. After a further 10 minutes the tubes are centrifugalized, and the degree of haemolysis is assessed by comparing the amount of haemoglobin in the supernatant fluid matched against a series of standards made from the actual blood used for the test. These standards are prepared as follows. To 100 drops of distilled water are added 4 drops of blood. Of this haemoglobin solution, 20, 16, 8, 4, 2, and 1 drops are placed in a series of tubes and the volume of each is made up to 25 drops. The series then contains an amount of haemoglobin equivalent to 80, 64, 32, 16, 8, and 4 per cent of haemoglobin in the actual test. The supernatant fluid in the test proper can be compared with these standards against a piece of white paper. The following are the observed limits of normal variation, using Creed's technique:

NaCl per cent –	0·28	0·32	0·36	0·40	0·44
Haemolysis per cent –	98-100	90-98	45-90	10-46	0-10

BILIRUBINAEMIA

Determination of Plasma Bilirubin

The principle of this method is colorimetrical comparison of the red colour produced by bilirubin in the presence of diazotized sulphanilic acid with an artificial standard containing methyl red.

Diazo-reagents. Solution A: 1 g. of sulphanilic acid is dissolved in 250 c.cm. of N hydrochloric acid and diluted to 1 litre with water. Solution B: 0·5 g. of sodium nitrite in 100 c.cm. aqueous solution. The reagent is freshly prepared, as required, by mixing 0·3 c.cm. of solution B with 10 c.cm. of solution A.

Standard.—Stock Methyl Red Solution. 0·29 g. of pure methyl red is dissolved in glacial acetic acid, and diluted with the same acid to 100 c.cm. Standard Methyl Red Solution: 1 c.cm. of the above stock solution, 5 c.cm. of glacial acetic acid, and 14·4 g. of crystallized sodium acetate are made up to 1 litre with water. This solution, at *p*H 4·63, contains 2·9 mg. of methyl red per litre, and matches the colour obtained when 0·1 mg. of bilirubin is treated with diazo reagent in a final volume of 25 c.cm.

Method.—Quantitative reaction. 1 c.cm. of plasma or serum is treated in a centrifuge tube with 0·5 c.cm. of diazo reagent, 0·5 c.cm. of saturated ammonium sulphate, and finally 3 c.cm. of absolute alcohol. The mixture is stoppered, thoroughly shaken, and filtered after a few minutes. The colour of the filtrate is matched against the standard in the colorimeter, using a green-light filter. The reading of the standard divided by the reading of the unknown and multiplied by 1·6 gives the mg. of bilirubin per 100 c.cm. of plasma or serum: 1 mg. of bilirubin equals 2 units.

Direct reaction.—If the diazo reagent is carefully 'layered' above the plasma and the tube allowed to stand for a few moments, a positive 'direct' reaction is shown by a red colour at the liquid junction.

The normal level of plasma bilirubin obtained by this method varies from 0·2 to 1·7 mg. per 100 c.cm., although most normal results are below 0·8 mg. per 100 c.cm.

MISCELLANEOUS

HAEMOGLOBIN DERIVATIVES

Methaemalbumin (pseudo-methaemoglobin)

169 This pigment is found in blackwater fever and other haemolytic anaemias (Fairley and Bromfield, 1937, 1939); it is similar in structure to methaemoglobin except that the pigment is combined with plasma albumin instead of globulin; it is extracorpuscular and cannot act as a respiratory pigment. Only the serum albumin of human beings and monkeys can form this substance. The spectrum closely resembles that of methaemoglobin, but careful examination has shown that the α band is at 6240, instead of at 6300, as in the case of methaemoglobin.

Creed, F. ff. (1938) *J. Path. Bact.*, **46**, 331.
Davidsohn, I. (1938) *Amer. J. clin. Path. Tech. Suppl.*, **2**, 56.
Fairley, N. H., and Bromfield, R. J. (1937) *Trans. R. Soc. trop. Med Hyg.*, **31**, 139.
(1939) *ibid.*, **32**, 431.
Hynes, M., and Whitby, L. E. H. (1938) *Lancet*, **2**, 249.
Ivy, A. C., Shapiro, P. F., and Melnick, P. (1935) *Surg. Gynec. Obstet.*, **60**, 781.
King, L. J., Haslewood, G. A. D., and Delory, G. E. (1937) *Lancet*, **1**, 886.
Paul, J. R., and Bunnell, W. W. (1932) *Amer. J. med. Sci.*, **183**, 90.
Tocantins, L. M. (1938) *Medicine, Baltimore*, **17**, 155.

BLOOD PRESSURE, HIGH AND LOW

See also Surveys and Abstracts 1939, pp. 65 and 248.

HIGH BLOOD PRESSURE

Aetiology

170 In a lecture on the problem of high blood pressure, Pickering discussed the claims for the various hypotheses of causation of high blood pressure in (i) essential hypertension, (ii) acute and chronic nephritis, and (iii) coarctation of the aorta.

In all these conditions the rise is due to vasoconstriction, probably uniformly distributed and involving the small arteries and arterioles. Of the 3 possible causes of this constriction, namely (*a*) structural changes in the blood vessels, (*b*) nervous, and (*c*) chemical influences, the evidence in support of (*a*) and (*b*) is insufficient.

The third possibility (*c*), namely that the vasoconstriction is of chemical origin, is supported by the following experiments (Prinzmetal and Wilson, 1936; Pickering, 1935, 6). The flow of blood in any organ is proportional to the perfusing pressure divided by the resistance offered by the vessels. In persistent hypertension the blood-flow through the upper extremity is normal, i.e. the increased pressure is balanced by increased vascular resistance. The vasomotor nervous tone in essential, malignant, and chronic nephritic hypertension can be removed by raising the body temperature. When this was done there was not any increase in the flow of blood through the forearm; this showed that the vasomotor nervous tone is not the abnormal factor, and that this is probably chemical in origin. In coarctation of the aorta the results obtained by Prinzmetal and Wilson and by Pickering were discordant. If essential hypertension is due to a chemical pressor substance, it might be expected that intravenous injection of extracts of the blood or of blood into the circulation of normal or, as in Pickering's hands, anaemic persons would raise the blood pressure; this has not been shown to be constant. There is evidence that the kidney might be the source of such a pressor substance; in 1896 Tigerstedt and Bergman obtained from the normal renal cortex a protein-like pressor substance, renin. If such a pressor substance is responsible for hypertension it must be small in amount, relatively stable in the body, and fixed to the vessels on which it acts.

Goldblatt summarized his own work since 1928 and that of others on the experimental production of arterial hypertension by renal ischaemia. Mechanical narrowing by a clamp of the main renal artery of one or both kidneys and of the aorta above or below the origin of the renal arteries, was performed. Constriction of the main renal artery of one kidney caused hypertension for some weeks, but usually for not longer than a month. Adequate constriction of the main renal arteries of both kidneys led

to permanent hypertension, both systolic and diastolic; in some of the animals the hypertension had persisted at a high level for more than 5 years. The same effect followed constriction of the main renal artery on one side and subsequent removal of the other kidney. All these investigations directed to the study of the pathogenesis of experimental hypertension have given results indicating the existence of a humoral mechanism of renal origin, which is responsible for the vascular constriction and the consequent increased peripheral resistance which causes hypertension. There was not any proof that there was a nervous reflex from the ischaemic kidney. In some dogs such an extensive collateral circulation had taken place around the kidneys that both the main renal arteries had been finally occluded completely, and the animals survived for several years with very high blood pressure but without any accompanying significant impairment of renal function. A very cautious suggestion was made that the production of vascular adhesions around a kidney with an obstructed renal artery, if this diagnosis could be made, might be beneficial in hypertensive patients. 170

Fishberg (1939) discussed the aetiology of essential hypertension under 3 headings, (i) renal factor, which before Goldblatt's work would not have received support, (ii) endocrine factors, adrenal and pituitary (Cushing's syndrome), and (iii) environmental factors, due to civilization. Fishberg prefers the longer title of the 'malignant phase of essential hypertension' to the shorter ones of 'malignant hypertension' or 'malignant sclerosis' and lays stress on the causal importance of long continued and extremely high diastolic blood pressure in the production of acute damage in the renal arterioles, and necrosis of the glomerular tufts present in the malignant phase of essential hypertension. W. Evans and O. Loughnan analysed the effects of 33 drugs or preparations, including nitrites, iodides, sedatives, xanthine and choline derivatives, vegetable extracts, and hormones, on the blood pressure and symptoms of 70 persons with hyperpiesia (essential hypertension). After elimination of possible fallacies and comparison with control cases given placebos, it appeared that none of the 33 preparations had a hypotensive effect on the patients with essential hypertension. Symptomatic improvement, more than that due to placebos, followed the use of 6 preparations only, namely bismuth subnitrate, iodine and iodides, bromides, phenobarbitone sodium, theominal (theobromine and phenobarbitone), and potassium thiocyanate

Evans, W., and Loughnan, O. (1939) *Brit. Heart J.*, **1**, 199.
Fishberg, A. M. (1939) *Hypertension and Nephritis*, p. 613
Goldblatt, H. (1938) The Harvey Lectures, Ser. 33, 237, Baltimore. (1935–6) *Clin. Sci.*, **2**, 208, 363
Pickering, G. W. (1939) *Brit. med. J.*, **1**, 1
Primmetal, M., and Wilson, C. (1936) *J. clin. Invest.*, **15**, 63
Tigerstedt, R., and Bergman, P. G. (1898) *Skand. Arch. f. Physiol.*, **8**, 223.

BLOOD TRANSFUSION

See also Surveys and Abstracts 1939, p. 250

DETERMINATION OF BLOOD GROUPS

The 'ABO' or international system of nomenclature has now been adopted by the British Red Cross donor service and will soon be used exclusively in Great Britain. 172

The two group substances A and B have been found to consist of protein and carbohydrate fractions. They might be extracted from living red cells in aqueous or alcoholic solution. Immunologically they act as haptenes, i.e. when combined with a protein they are true antigens and can provoke specific antibodies (agglutinins). When extracted and separated from the natural protein, they lose their power to provoke antibodies, but can still be detected by reacting specifically with a serum already containing the antibodies. In this way it has been shown that these group substances are not possessed by red cells alone but are distributed throughout the body and present in every tissue and secretion.

TECHNIQUE OF TRANSFUSION

Blood Transfusion in War Time

The impossibility of obtaining at very short notice in war time a sufficient supply of living donors, either in the field or in towns under aerial bombardment, has

172 resulted in much work upon the use of stored blood and the institution of 'blood banks'. Two sources of blood are available, living donors and blood from the placenta. The yield of placental blood is small, and contamination is often difficult to avoid. Living donors are the only practicable source on the large scale. Bloods may be collected with the strictest aseptic precautions into closed, and finally sealed, bottles containing 3 per cent citrate, which are stored at 2° C. The blood must not freeze, because it becomes toxic on thawing. It must be kept in the dark, and not be agitated, otherwise early haemolysis occurs; in any case, under the most favourable conditions, haemolysis commences within a week, and at least mild rigors may be expected from transfusions with blood stored for more than one week. The approximate figures are: with blood stored 1 week, reactions 10 per cent; 2 weeks, reactions 20 per cent; 3 weeks, reactions as frequent as 40 to 50 per cent. Attempts to improve these figures are now being made by varying such factors as the anticoagulant, methods of bottling, and conditions of storage. In order to avoid minor incompatibility, the principle of mixing at least 6 bloods of the same group was adopted during the Spanish civil war, and in this way, by using only universal donors, preliminary grouping was altogether avoided. But, if the stored blood is not of the mixed universal donor type, then the usual preliminary grouping and cross matching must be done. At the time of collection each bottle of blood should be accompanied by two smaller samples from the patient, one (clotted) for a Wassermann reaction and one (citrated) for grouping. From the storage bottle the blood may be transfused by any of the methods usually employed for fresh blood or, if great speed is necessary, a positive pressure may be created inside the storage bottle, and allowed to drive the blood directly through a tube and a needle into the patient's vein. For this rapid work, numerous devices are now being tried. The following are the chief

Withdrawal of Blood from Donor

In all cases a closed negative pressure (suction bulb) apparatus is used. The screw-capped U.G.B. bottle and the metal 2-way top suggested by McCartney serve admirably. The bloods can be stored singly, or 6 may be mixed and rebottled by any strictly aseptic means. By exchanging the cap for one carrying a rubber bulb giving light positive pressure the blood can be transfused directly from the same bottle, and, if the bottle is kept raised or suspended above the arm level, the syphonage produced by its height above the arm will cause the transfusion to continue, even though the bulb is removed. The operator can then proceed to the next patient and start a second transfusion, and so on.

Another method, also using the U.G.B. screw-capped bottle, is as follows. Under the cap of the bottle is a thick solid rubber washer, and the cap itself has a central small perforation. The bottles are autoclaved with the cap loose, the cap is then tightened before it is completely cold, with the result that good permanent negative pressure within the bottle is obtained. The bottles are stored in this condition. The donor's vein is pricked with a needle to which is attached a rubber tube with a needle also at its other end (all sterilized). Immediately the vein is entered, the distal needle is thrust through the central hole in the cap of one of the vacuum bottles, into which the blood is thus collected. The bottle of blood is then stored, or mixed with 5 others and then stored as before. The blood may be administered by any of the methods described already, or by a quick emergency method thus:

By blowing in several syringefuls of air from a sterilized syringe, repeatedly puncturing the cap, a strong positive pressure is produced inside the bottle. Using a sterile rubber-tube with a needle at each end as before, the patient's vein is punctured by one needle and the rubber cap with the other, the bottle being held inverted; the blood at once flows.

BOILS AND CARBUNCLES

CARBUNCLES

Treatment

174 The treatment of severe carbuncles by X-rays has been reported on by O'Brien and by Meyer. O'Brien gave the results in 130 patients treated in the Boston City Hospital; 4 of these died, giving a mortality of 3 per cent. The lesions were situated on the back of the neck (53), upper lip (28), lower lip (7), cheek (16), shin (6), back

(7), and elsewhere (13). X-ray therapy with dry dressings only was given to 60 patients; the others had surgical treatment either before or after the X-rays. Convalescence was shorter in the first group of 60 than in the others. According to O'Brien diabetes mellitus does not contra-indicate X-ray therapy. Meyer also advocated very moderate doses of X-rays (between 10 and 200 *r*) to check the development of a carbuncle. In very severe cases he advised additional treatment with antiseptic powders and a vaccine. Both authors pointed out that X-rays do not relieve the pain immediately. 174

Meyer also advocates short-wave therapy, either alone or combined with X-rays; if both methods are used they should not both be given on the same day. The wavelength is not important, but the intensity must be moderate, particularly when the lesions are most acute. The duration of treatment varies between 10 and 30 minutes. Treatment is repeated daily; Meyer finds that 2 to 4 treatments are necessary for a furuncle and about a dozen for a large progressing carbuncle on the neck.

Meyer, J. (1939) *Brit. J. phys. Med.*, N.S. **2**, 72.
O'Brien, F. W. (1939) *New Engl. J. Med.*, **220**, 917.

BONE DISEASES

See Surveys and Abstracts 1939, p. 253. 175-184

BORNHOLM DISEASE

Aetiology

Weterings recorded 3 cases of Bornholm disease in Holland, admitted to hospital as cases of acute appendicitis, perforated peptic ulcer, and diaphragmatic pleurisy respectively, and reviewed the subject, especially the aetiology. As bacteriological examinations of the blood, cerebrospinal fluid, and smears from the nose and nasopharynx had been constantly negative a virus seemed to be probably responsible, and a similarity between acute poliomyelitis and Bornholm disease was mentioned. The disease mainly occurred in young children and adolescents; the onset was acute, the symptoms passing off in 24 hours but very often returning on the third day. 185

Clinical Picture

Pickles has given a summary of his experience of the disease which had been variously named as Bornholm disease, epidemic myalgia, epidemic myositis, and locally in the United States as the 'devil's grip'. With an experience of 5 small epidemics he had seen 31 cases, 15 being in children under 11 years of age in whom the symptoms were more severe than in adults. Three points were useful in diagnosis in children: (i) the almost invariable absence of vomiting, thus helping to rule out acute abdominal lesions, especially appendicitis, (ii) the greatly increased respiratory rate, whether the pain is thoracic or abdominal, and (iii) the rarity or absence of cough. A striking feature was the intermittent character of spasmodic pain with intervals of well-being. Pneumonia might be simulated. One attack did not prevent a second. The Danish describer of Bornholm disease, Ejnar Sylvest, had informed Pickles that the disease had disappeared from Denmark.

Pickles, W. N. (1939) *Epidemiology in Country Practice*, Bristol, p. 87.
Weterings, P. A. A. (1939) *Ned. Tijdschr. Geneesk.*, **83**, 2326.
— (1939) *Lancet*, **2**, 146.

BRAIN ABSCESS

See Surveys and Abstracts 1939, p. 254. 187

BRAIN: REGIONAL DIAGNOSIS

See Surveys and Abstracts 1939, p. 255. 188

BRAIN TUMOUR

See Surveys and Abstracts 1939, pp. 94 and 257. 189

BREAST DISEASES

191-197 See Surveys and Abstracts 1939, p. 260.

BRONCHIECTASIS, BRONCHIOLECTASIS, AND BRONCHIAL SPIROCHAETOSIS

See also Surveys and Abstracts 1939, p. 265.

BRONCHIECTASIS

AETIOLOGY

199 Various authors recently supported the hypothesis that atelectasis or collapse played an important part in the causation of bronchiectasis. It has been pointed out that the normal degree of negative intrapleural pressure was greatly increased by the presence of a collapsed lobe on the same side; a pressure of - 432 mm. of water had been recorded in a case of massive collapse of a lung. It was believed that, in the absence of alveolar dilatation in response to this dilating force, the bronchi were dilated by a 'compensatory' dilatation. Jennings reviewed the reports of observations supporting this hypothesis published up to the end of 1937, and described a new case. In a man, aged 35, a lipiodol radiograph showed cylindrical dilatation of the bronchi of the left lower lobe; there was also evidence of atelectasis of the left lower lobe, probably caused by accumulated mucus. Later, sputum was coughed up, and the lobe re-expanded. The bronchi then returned to their normal width. In view of his conclusions, he urged the necessity of promoting early re-expansion of a collapsed lobe.

Lander and Davidson (1938, a) strongly supported this view, and emphasized that the bronchi, in spite of their being dilated, had not lost their elasticity. They compared radiographs from bronchiectatic patients taken in full inspiration and in complete expiration in the same patients, and found that the calibre of the dilated bronchi was significantly less in the stage of expiration than on inspiration, when the negative pressure in the pleural cavity was greater. This diminution in size was more prominent in ectactic than in normal bronchi, and demonstrated that the elastic tissue, and elasticity, of the bronchioles were not impaired. In one of their cases there was radiological proof of bronchiectasis for 10 years, but, even in this case, the bronchograms showed that in the expiratory stage the bronchi were almost normal. Lander and Davidson further expressed the opinion (1938, b) that pulmonary collapse was a necessary and invariable antecedent of all bronchiectasis, and insisted that the hypothesis of infection was no longer tenable.

TREATMENT

Churchill strongly advocated lobectomy or pneumonectomy for bronchiectasis, because the condition was progressive and often fatal, and the only real cure was extirpation of the diseased section of the lung. In 1937 he described the results from lobectomy and pneumonectomy, the mortality rates were as follows. In 49 patients treated by lobectomy or pneumonectomy for bronchiectasis or cystic disease, 6·1 per cent. In 40 patients treated by lobectomy for bronchiectasis and cystic disease, 5 per cent. In 38 patients treated by lobectomy (1 bilateral) by the latest devised method, 2·6 per cent. (i.e. 1 death). In 1938 he reported a total of 84 cases of bronchiectasis treated by lobectomy with a mortality of 4·7 per cent. All the surviving patients were benefited.

Romanis and Sellors considered that the choice of patients suitable for operation depended upon localization of the condition to one lobe and on the general condition of the patient.

Churchill, E. D. (1937) *J. thorac. Surg.*, **6**, 286.
—— (1938) *New Engl. J. Med.*, **218**, 97.
Davidson, M. (1939) *Practical Manual of Diseases of the Chest*, 2nd ed., in press.
Jennings, G. H. (1937) *Brit. med. J.*, **2**, 963.
Lander, F. P. L., and Davidson, M. (1938, a) *Brit. med. J.*, **1**, 1047.
—— (1938, b) *Brit. J. Radiol.*, **11**, 65.
Romanis, W. H. C., and Sellors, T. H. (1936) *Lancet*, **2**, 1445.

BRONCHITIS AND BRONCHO-PNEUMONIA

See also Surveys and Abstracts 1939, p. 266.

BRONCHO-PNEUMONIA

Treatment

The following additional therapeutic measures are generally considered valuable: (i) blood transfusions in infants with severe broncho-pneumonia; (ii) bronchoscopy in broncho-pneumonia, when there is a possibility of pulmonary collapse from bronchial obstruction, especially post-operative and coma cases, (iii) short-wave diathermy to the chest in broncho-pneumonia with delayed resolution, and in certain cases of chronic bronchitis. 205

Since 1935, when Domagk published a paper on the value of prontosil in experimental streptococcal infection, there has been a remarkable advance in chemotherapy with the sulphonamide group of drugs: new compounds are constantly being prepared and tested but the ideal drug is still to be produced. Whitby found that 2-sulphanilyl-aminopyridine (M & B 693) protected mice against certain strains of pneumococci, and its clinical value in pneumonia was investigated by Evans and Gaisford. Subsequently many papers have been published confirming the therapeutic value of this drug in pneumococcal and other infections. At the moment M & B 693 is probably the most widely used member of the sulphanilamide group in Great Britain; indeed it is being used so freely in all sorts of undiagnosed febrile illnesses that it is likely that it may be brought into undeserved disrepute in view of its toxic properties. Nausea, vomiting, and diarrhoea are commonly produced by it, but peripheral neuritis, agranulocytosis, and haematuria have also been reported (Browning).

In the treatment of pneumonia with the drug, some observers have found an undue proportion of unresolved pneumonia and empyemas, and it is possible that the natural production of immunity may be interfered with in some way by the rapid destruction of the bacteria in the body.

While noting these disadvantages, M & B 693 and similar compounds are most valuable therapeutic agents in acute infections of the respiratory tract and should be prescribed in certain cases of broncho-pneumonia and acute bronchitis: except in very acute infections, it may be advisable to withhold the drug for 48 to 72 hours after the onset, with the idea of allowing the processes of natural immunity to begin. The drug should be prescribed in adequate dosage, an average adult requires an initial dose of 2 g. followed by 1 g. every 6 hours until the temperature falls, and then 0·5 g. every 6 hours for 3 to 5 days. Infants tolerate the drug well and require rather a larger dose per body weight than adults.

Browning, C. H. (1939) *Brit. med. J.*, **2**, 267.
Domagk, G. (1935) *Dtsch. med. Wschr.*, **61**, 250.
Evans, G. M., and Gaisford, W. F. (1938) *Lancet*, **2**, 14.
Whitby, L. E. H. (1938) *Lancet*, **1**, 1210.

BRONZING OF THE SKIN

See also Surveys and Abstracts 1939, p. 267.

PIGMENTATION DUE TO PHYSICAL AND CHEMICAL CAUSES

Pitch dust and fumes.—The pigmentation so common in trades connected with the distillation of coal tar, and in the various subsidiary processes involving contact with pitch, e.g. road-spraying, is probably an example of a combined chemical and physical cause, for undoubtedly the dermatitis usually preceding or accompanying the pigmentation is always aggravated by sunlight, as is berloque dermatitis. The areas exclusively affected are the face, arms, and neck, whereas covered parts invariably escape. The chemical substances responsible might therefore be regarded as photosensitizers and it is reasonable to suppose that, if such subjects were never exposed to daylight, neither dermatitis nor bronzing would develop. Observations were made in a factory of the clinical effects of pitch, used in combination 208

208 with asbestos for the manufacture of electrical insulators, switchboards, and fountain pens. The mixture was raised to a high temperature in open cauldrons and manipulated and tended by hand; the operators all had a strikingly swarthy appearance, and dermatitis, more or less active, of the extensive surfaces of the body exposed. A few of the men were occasionally sent for treatment of the 'warts' on the face and backs of the hands (tar mollusca) to which workers in all such occupations are liable. One of them presented himself 8 years later with an epithelioma on the cheek, and, although he had long since abandoned his work among the fumes, was still characteristically and deeply bronzed on the face, neck, and hands. The patient was photographed in natural colour and the photograph is preserved (Semon and Moritz) as an example of both the early and late results of exposure to the fumes of boiling pitch

Berloque dermatitis.—That the sun or ultra-violet rays were not essential in the production of pigmentation in the course of berloque dermatitis was suggested by the following case. A man, aged 64, presented himself with dermatitis and pigmentation below, but not involving, the left nipple and spreading with a rather defined margin downwards and towards the umbilicus. A similar condition involved the skin of the left upper arm. He was in the habit of wearing a handkerchief in the pocket of his pyjama coat and for some 3 years had sprayed it almost nightly with eau-de-Cologne. A patch test with a single drop of the scent elicited an acute reaction on the front of the right thigh within 24 hours, thereby proving the cause of his symptoms; the condition rapidly cleared up with simple treatment; the slaty pigmentation, however, persisted for several weeks. As the patient had never indulged in sun-bathing, and not even in sea-bathing for 10 years, the influence of ultra-violet light might be definitely excluded

PIGMENTATION DUE TO CONSTITUTIONAL CAUSES

The direct aetiology of the pellagra syndrome is still a matter of doubt and, although a B_1 avitaminosis is the most often incriminated, there is some evidence that this deficiency is not the sole explanation (Murray). This hypothesis does not account for the preponderance of cases in women—a fact which might suggest an endocrine involvement as well as a simple deprivation of vitamin.

Hyperpigmentation might occur in toxic goitre, Addison's disease, and other syndromes such as scleroderma in which there is an undoubted disturbance of endocrine function. Vitamin C is normally present in the adrenal cortex, and deficiency of vitamin C leads to hypertrophy of the cortex and diminished production of adrenaline. If therefore adrenaline and melanogen are derived from the same source this would result in more melanogen reaching the skin. Quoting Szent-Gyorgyi, Goldsmith stated that vitamin C as a reversible reducing agent was capable, in even minimal concentration, of completely inhibiting the formation of pigment. Subjects of Addison's disease lost some of their pigmentation when treated with natural ascorbic acid (vitamin C) and recently a patient with scleroderma, marked hyperpigmentation about the wrists and neck, and cutaneous calcinosis notably improved as regards the melanosis after 6 weeks on a combined medication of ascorbic acid and adrenaline, although the sclerodermatous changes remained much as they were.

Goldsmith, W. N. (1936) *Recent Advances in Dermatology*, London, p. 488.
Murray, I. (1936) *Glasg. med. J.*, **125**, 49
Semon, H. C. G., and Moritz, A. (1939) *An Atlas of the Commoner Skin Diseases*, 2nd ed., Bristol.

BURNS AND SCALDS

209 See Surveys and Abstracts 1939, p. 267.

CAISSON DISEASE

210-211 See Surveys and Abstracts 1939, p. 270.

CANCER

See also Surveys and Abstracts 1939, pp. 28 and 270.

PATHOLOGY AND AETIOLOGY

Carcinogenic Action of Rabbit Papilloma Virus on Tarred Skin of Rabbits

212

Rous (1936) reviewed the position at that date of the tumour problem as it concerned man and animals from the point of view of the tumours known to have a virus causation. He traced the progress of ideas since the transplantation of chicken tumours was first successfully accomplished 25 years previously. This was followed by the separation from the tumour cells of a causal agent which could similarly induce the growth of tumours in healthy fowls. It was then recognized that the potentiality of inducing cell proliferation was not altogether contrary to the usual properties of viruses, but that viruses could be ranged in a graded series, with at one end those causing necrosis of the cell (e.g. foot and mouth disease) and at the other end those causing proliferation. The next advance was the discovery of a mammalian tumour which was similarly caused by a virus -namely, the Shope papilloma of cotton-tail rabbits. The importance of this tumour has greatly increased since the discovery by Rous and Beard that under certain conditions these benign papillomas became malignant. When transplanted into domestic rabbits these tumours grew more vigorously than in the cotton-tail rabbit, this might be because the relation between the virus and its natural host had become balanced and almost of the nature of a symbiosis, whereas the domestic rabbit had no such tolerance. Rous and Beard found that the most vigorously growing tumours had malignant potentialities and that, when 10 animals carrying such tumours were kept for a sufficiently long time (200 days), cancer developed in 7 of them. They mentioned the analogy to human papillomas which become malignant. Rous discussed in detail the parts played in the cancerous change by various factors, such as cell injury, the virus, the host cells, and circulating antibodies in the host. He concluded with a summary of the difficulties which apparently stood in the way of the assumption that malignant growths in general were due to viruses, and decided that they were not fundamental obstacles.

In a later paper (1938) Kidd and Rous reported that preliminary tarring of the ears of rabbits, before injection into the blood stream of rabbit papilloma virus, localized the resultant growths to the ears and was followed by the development of malignancy within about a fortnight. The nature of the cellular changes that might determine the development of these anomalous tumours was discussed. Tarring the anomalous tumours hastened the process of anaplasia but, on the other hand, tarring ordinary papillomas failed to favour their development into carcinomas. These anomalous tumours did not develop from ordinary papillomas but were evoked by the carcinogenic stimulus provided by the virus to the tarred skin; in some cases pre-existing tar tumours were spurred to malignancy.

Extra-chromosomal Influence in the Transmission of Mammary Tumours of Mice

Bittner and other members of the staff of the Roscoe B. Jackson Memorial Laboratory advanced the hypothesis that mammary tumours in mice were determined by an extra-chromosomal influence (Bittner, 1936). Bittner and Little (1937) reported further experiments in support of this view. They found on the other hand that lung tumours in mice were determined in accordance with genetic principles. Bittner (1937) discussed the 3 possible hypotheses to explain the peculiar features in the inheritance of these mammary tumours in mice. It had previously been shown that the incidence of such tumours was greater when the mother came of a high-tumour stock than when the father came of such a stock. Bittner reared the female progeny of a female from a high-tumour stock by fostering them with females of a low-tumour stock and found that the incidence of mammary tumours was reduced, although the fostered mice lived longer than the controls and therefore more of them lived to the age at which cancer develops. He concluded that the extra-chromosomal influence active in the transmission of these mammary tumours was transmitted through the mother's milk. In a more recent paper Bittner (1939) found that, by his method of fostering mice of high breast-tumour stock, the incidence of cancer was reduced from 83·6 per cent in the stock to 7·4 per cent when the young are removed from their mothers within the first 24 hours after birth. The breeding

212 of the fostered mice is to continue actively in the investigation of the incidence of cancer in their progeny. He stated that the nature of the 'breast-cancer-producing' influence—hormonal, chemical, or virus—has not been determined.

Carcinoma in Leopard Frog probably caused by a Virus

A new tumour occurring in the leopard frog (*Rana pipiens*) and caused by a specific virus has been described by Lucké. This was an epithelial tumour of the kidney with all gradations from a benign adenoma to a malignant and invasive adenocarcinoma. In the cell nuclei, acidophilic inclusions resembling those in other virus diseases were common. Metastases, most frequent in the liver, also occurred in the pancreas, intestine, peritoneum, mesentery, ovary, retroperitoneal tissue, bladder, lung, and eye, dissemination usually taking place by the blood stream. The tumour could be transmitted by inoculation of living tumour or of desiccated or glycerinated tumour. The tumour could not be transmitted to alien species of frogs.

Bittner, J. J. (1936) *J. Hered.*, **27**, 391.
(1937) *Amer. J. Cancer*, **30**, 530.
(1939) *Amer. J. Cancer*, **35**, 90.
and Little, C. C. (1937) *J. Hered.*, **28**, 117.
Kidd, J. G., and Rous, P. (1938) *J. exp. Med.*, **68**, 529.
Lucke, B. (1938) *Amer. J. Cancer*, **34**, 15.
(1938) *J. exp. Med.*, **68**, 457.
Rous, P. (1936) *Amer. J. Cancer*, **28**, 233.
and Beard, J. W. (1935) *J. exp. Med.*, **62**, 523.

CANCRUM ORIS

Treatment

213 For treatment of stomatitis see APHTHOUS FEVER, p. 25.

CARRIERS IN INFECTIVE DISEASE

CARRIERS IN SPECIAL DISEASES

Streptococci

215 During the last few years attention has been directed to the spread of virulent haemolytic streptococci in hospital wards. In some instances individuals throughout the hospital, both among the patients and in all grades of the personnel, have become infected in the course of some weeks, and investigation has shown that, besides overt cases of such conditions as tonsillitis, a number of symptomless carriers have formed links in the chain of infections. Such an 'epidemic' has even led to deaths, especially in marasmic infants, and has been associated with cases of acute rheumatism following in the wake of the more obvious streptococcal infections. Convalescents and carriers discharged from hospital have also taken infection to their homes (Bradley). Similar infections spread by carriers are especially liable to occur in wards where throat and nasal cases are treated (Okell and Elliott). It has long been recognized that the infection of wounds at operations and in lying-in wards may be due to streptococci in droplets discharged from the mouth of a surgeon or nurse who is a carrier (Colebrook). It is advocated that masks should be used by those present at operations or attending cases of confinement to prevent the latter types of infection but, unless properly designed, the masks may be ineffective. Examination of the throats of attendants for virulent forms of streptococci is an important prophylactic measure.

Staphylococci

Careful observations and experiments have shown that surgeons may unwittingly 'carry' virulent staphylococci on the apparently healthy skin and may infect operation wounds even through unnoticed minute holes in rubber gloves (Devenish and Miles).

Enteric Fever

Felix proved that chronic carriers of *Bacillus typhosus* can be detected by carefully testing their blood serum for agglutination of the 'Vi' form of this bacillus which contains the special 'Vi' antigen associated with virulence. Strains of this form can be isolated from acute cases of typhoid fever and from carriers, but some of the

strains are more suitable than others, and are used to make up the recognized suspensions prepared for this special agglutination test. The serum of those who have recovered from the disease, but are not carriers, does not give this agglutination reaction with 'Vi' antigen, but often agglutinates the formerly recognized H and O forms of the bacillus (Felix; Pijper and Crocker). 215

Herpes Zoster and Varicella

The connexion between herpes zoster and varicella may be mentioned as an instance of a carrier who does not in ordinary circumstances discharge the infective agent nor transmit the disease. According to the most plausible hypothesis, a person recovered from varicella retains the virus in the central nervous system or spinal ganglia and later in life (sometimes after many years, but only once in a lifetime) the virus descends the sensory nerves and produces vesicles on the skin which then disperse virus as if from a case of varicella, so that persons in contact become infected with the latter disease. This suggested explanation is not entirely satisfactory but is widely accepted

Bradley, W. H. (1938) *Brit. med. J.*, **2**, 733.
Colebrook, L. (1936) *Brit. med. J.*, **1**, 1257.
— (1938) *J. Obstet. Gynaec.*, **43**, 691.
Devenish, F. A., and Miles, A. A. (1939) *Lancet*, **1**, 1088.
Felix, A. (1938) *Lancet*, **2**, 738
Okell, C. C., and Elliott, S. D. (1935) *Lancet*, **2**, 869.
Pijper, A., and Crocker, C. G. (1937) *S. Afr. med. J.*, **11**, 113.

CATARACT

Vol. III

See Surveys and Abstracts 1939, p. 272. 216

CELLULITIS

TREATMENT

Sulphonamide drugs have been widely employed in cellulitis, and in many cases have been reported to improve the clinical condition within 48 hours. The prophylactic administration of the drug in the treatment of infected and dirty wounds has also been strongly recommended. 217

CELLULITIS, PELVIC

PELVIC CELLULITIS IN THE FEMALE

TREATMENT

Short-wave therapy Inflammatory diseases of the pelvis constitute one of the most important causes of chronic invalidism in women. During the last few years there has been a marked tendency to adopt conservative methods of treatment, rather than to resort to surgical operations, which have frequently to be repeated, and are often unsuccessful 218

For inflammatory tumours of the adnexa, adnexitis, parametritis, and pelvic cellulitis ordinary diathermy gave a measure of success, but is now being abandoned for short-wave therapy which, according to many authorities, is infinitely superior to the former. According to Justina Wilson the immediate effect of the application of short-wave therapy is freedom from pain, this relief occurring after one or two treatments. There follows improvement in all the subjective symptoms, with a definite fall in temperature. In recent cases of adnexal tumours, diminution in size occurs early, and all inflammatory exudate is gradually absorbed. During the past year Justina Wilson has treated with short-wave therapy over 60 cases of adnexal disease in the subacute stage. In most of these, cervical smears proved the presence of the gonococcus; in the others, a positive reaction for gonococci was not obtained, but there were many pus cells present, and in all cases there were subacute cellulitis and endocervicitis. The degree of pelvic involvement varied considerably, in some cases there were semi-thickened tubes, which were very tender and painful; in 5 cases of abortion there were large tubo-ovarian masses. All cases were treated by the usual abdomino-sacral technique, the vertical electrode completely covering the pelvis, and the dorsal protruding below the coccyx. Glass-shod metallic electrodes

218 about 18 cm. in diameter with a wide air-space were used. In placing the electrodes care was taken to ensure that all the organs of the true pelvis—the uterus, adnexa, parametric tissues, and bladder—were in the condenser field. The dosage given depended on the patient's reaction, but the energy output was kept low, and only the mildest degree of warmth was experienced by the patient. Daily treatments, with an occasional rest, were given, and the time of application was increased carefully up to 15 or 20 minutes. After 10 days the treatment was reduced to 3 times a week. The most satisfactory cases were those that were suffering from the first attack of gonorrhoeal adnexal inflammation, in all these cases the pelvic mass disappeared, and the patients were entirely relieved of all symptoms in a comparatively short time (after 14 to 15 treatments), and showed a striking improvement in their general health. In 4 cases the symptoms disappeared, but the adnexal mass could still be felt on palpation, these cases were successfully operated on, and their convalescence was much more rapid than is generally the case.

In chronic cases the dosage was higher; initial sessions of treatment were of 10 minutes' duration, given daily, and were increased to up to 30 minutes. The prognosis in such cases depends on whether the condition is chiefly the result of inflammation, or due to the presence of hyperplastic cicatricial tissue, chronic induration, and adhesions, which lead to deformity of the tubes. In the latter type of case short-wave therapy alone cannot, of course, effect a cure.

PELVIC CELLULITIS IN THE MALE

219 Pelvic cellulitis is a not uncommon complication of operations for removal of carcinoma of the rectum. When it occurs the incision should at once be opened up (i.e. the stitches removed). The large gaping wound should be treated by free irrigations with mild antiseptics and light gauze packing. The head end of the bed should be raised to facilitate drainage. Several cases of injury to the rectum produced by rigid enema nozzles and followed by pelvic cellulitis have been recorded. Free drainage through the wound is valuable, and it may be necessary to divide the sphincter and rectal wall right up into the wound. Temporary colostomy has also proved valuable. In all forms of cellulitis that are slow in yielding to ordinary surgical measures sulphanilamide (or prontosil or M & B 693) may prove a useful adjunct.

Wilson, J. (1939) *Brit. J. phys. Med.*, 2, 208.

CEREBELLAR DISEASES

220 See Surveys and Abstracts 1939, p. 273.

CEREBRAL DIPLEGIA

221 See Surveys and Abstracts 1939, p. 273.

CEREBRO-RETINAL SYNDROMES OF THE HEREDO-DEGENERATIVE TYPE

ALLIED CONDITIONS

The Laurence-Moon-Biedl Syndrome

222 Sorsby, Avery, and Cockayne reviewed the new information on this syndrome reported between 1935 and the end of 1938. During this period 3 cases were reported from Japan and one from Egypt, whereas all previous patients have been of the Caucasian race. Necropsy findings have been reported in 3 cases, and preliminary notes in 2 others, but no significant lesion has been found. The range of clinical symptoms and associated conditions were discussed, and the information concerning the inheritance of the condition and the 2 hypotheses regarding its causation were summarized, (i) that one gene produces all the signs, and that incompleteness of the syndrome is due to the action of modifying genes; and (ii) that the syndrome is determined by 2 or more genes. Support was given to the hypothesis that the condition is determined either by 2 recessive genes on the same chromosome, or by some chromosomal error such as a dislocation or translocation.

Sorsby, A., Avery, H., and Cockayne, E. A. (1939) *Quart. J. Med.*, N.S. 8, 51.

CEREBROSPINAL FEVER

See also Surveys and Abstracts 1939, p. 274.

TREATMENT

223 *Sulphanilamide.*—Important advances have been made in the use of sulphanilamide and its derivatives. Buttle, Gray, and Stephenson were the first to test its action experimentally on animals by measuring its protective effect after intraperitoneal injections of meningococci. Schwentker, Gelman, and Long recorded the first clinical observations, treating 11 cases, with one death. They injected intrathecally 10 to 30 c.cm. of a 0·8 per cent solution of sulphanilamide in saline. They also injected subcutaneously 100 c.cm. for each 40 lb. (18 kg.) of body weight. Good results have been recorded by numerous observers subsequently. There is uncertainty as to the best dosage and methods of administration. The position was reviewed by Whitby in the Bradshaw Lecture. In meningococcal meningitis sulphanilamide is more active than sulphamido-chrysoidin (prontosil rubrum) or prontosil soluble and is effective in both Group 1 and Group 2 infections. The concentration of sulphanilamide in the spinal fluid should reach 5 mg. per 100 c.cm. in the first 24 hours and be maintained at this level for 3 days. This can be achieved by oral or subcutaneous administration. Lastly cyanosis is not an indication for reduction of the dose. Banks provided a critical report on the optimal method of treatment, based on 113 cases. He obtained good results by oral administration. This has been confirmed by other authors. Whether serum should be used to supplement sulphanilamide, and, if so, which type of serum—antitoxic or antibacterial—cannot confidently be stated. Experimentally, a combination of serum and sulphanilamide had been more effective than either alone, and clinical evidence was in favour of supplementing the drug with serum intravenously or intraperitoneally in severe cases; Banks's results indicated that, in mild cases between 5 and 20 years of age, the drug alone was sufficient. Chronic cases responded badly. Meningococcal septicaemia was equally amenable to treatment.

M & B 693.—Hobson and MacQuaide reported good results from M & B 693. In most of their cases the drug was given by the mouth only, in doses of 1 g. every 4 hours until symptoms were ameliorated. Serum was not injected.

Banks, H. S. (1933) *Lancet*, **2**, 7.
Buttle, G. A. H., Gray, W. H., and Stephenson, D. (1936) *Lancet*, **1**, 1286.
Hobson, F. G., and MacQuaide, D. H. G. (1938) *Lancet*, **2**, 1213.
Schwentker, F. F., Gelman, S., and Long, P. H. (1937) *J. Amer. med. Ass.*, **108**, 1407.
Whitby, L. (1938) *Lancet*, **2**, 1095.

CEREBROSPINAL FLUID

See Surveys and Abstracts 1939, p. 276 224

CERVICAL RIB

See Surveys and Abstracts 1939, p. 277 225

CHAGAS' DISEASE

AETIOLOGY

226 Many more cases of Chagas' disease have now been discovered in the various provinces in the Argentine, and Mazza reports that, although the total number of cases found between 1932 and 1936 was only 109, no less than 131 further cases had been recorded by June 1937. Although infected bugs are known to be widely distributed in Uruguay, no definite cases of the disease in man had been found up to 1936. An intensive search made during 1937 resulted in the discovery of about a dozen cases (Talice, 1937 and 1938).

Diagnosis

The Machado reaction as a diagnostic test has been further examined by Lacorte (1938) in Brazil, and by Johnsen and Kelser (1937) in Panama. Lacorte examined

226 the reaction in 35 patients who were suspected or definitely diagnosed to be cases of Chagas' disease. Positive results were obtained in 68·5 per cent of cases; in 35 control patients, including 30 who gave a positive Wassermann reaction and 5 who gave a negative Wassermann reaction, the Machado reaction was negative in every instance. Lacorte concluded that the Machado reaction, when properly carried out, afforded a valuable method of diagnosis of Chagas' disease.

Kelser (1936) introduced a modification of the Machado reaction, the essential feature of which was the use, as antigen, of a culture of the trypanosomes in a beef-peptone-agar medium, to which immediately before use a small quantity of a 0·1 per cent solution of dextrose and a little defibrinated guinea-pig blood were added. This modification of the Machado reaction was tested in more than 400 specimens of serum, including a number from known cases of Chagas' disease in man and animals. It proved positive in all known cases of the disease from which sera were available, and negative when there was no evidence of the disease. Johnson and Kelser made use of this technique in a survey of the incidence of Chagas' disease in Panama. Of 1,251 sera collected from various places in Panama, 37 were positive and 11 gave suggestive results. The infection rate as determined by the test was low for children under 15 years of age but rose sharply above this age. A possible explanation of this is the relatively high mortality from the disease in children. Johnson and Kelser concluded that the Machado reaction is of distinct value, not only in identifying active cases of Chagas' disease, but in revealing the incidence of the infection, past and present.

Johnson, C. M., and Kelser, R. A. (1937) *Amer. J. trop. Med.*, **17**, 385.
Kelser, R. A. (1936) *Amer. J. trop. Med.*, **16**, 405.
Lacorte, J. G. (1938) *Acta Med., Rio de Janeiro*, **1**, 264.
Mazza, S. (1937) *Festschrift Bernhard Nocht zum 80. Geburtstag von seinen Freunden und Schülern*, Hamburg, 305.
Talice, R. V. (1937) *Bull. Soc. Path. exot.*, **30**, 865.
(1938) *Arch. urug. Med.*, **12**, 645.
Alambarri, A., and Regules, U. (1938) *An. Fac. Med., Montevideo*, **23**, 761.
de Medina, F., and Rial, B. (1938) *An. Fac. Med., Montevideo*, **23**, 354.
Regules, U., and Alambarri, A. (1938) *Arch. urug. Med.*, **12**, 438.
Rial, B., and de Medina, F. (1937) *Arch. urug. Med.*, **12**, 497.
Volonterio, M., and Osmani, J. J. (1937) *Arch. urug. Med.*, **11**, 493.
and Terra-Nunez, G. (1938) *Arch. urug. Med.*, **12**, 241.

CHANCROID

See also Surveys and Abstracts 1939, pp. 155 and 277

TREATMENT

227 Batchelor and Lees reported good results from sulphonamide treatment. The dosage for men was 8 g. a day on the fourth and fifth days and 6 g. a day from the sixth to the ninth days. Possibly the dosage would now be smaller. Hanschell recommended prontosil soluble, 5 c.cm. of a 5 per cent solution given by deep subcutaneous injection, followed at 3-day intervals by one or two injections of 10 c.cm.; simultaneously 3 g. of prontosil album should be administered orally.

Lepinay (1939) reports on 4 groups of cases of chancroid: (i) those without adenitis, treated by oral administration of sulphanilamide; (ii) those without adenitis treated solely by local application of sulphanilamide, (iii) patients with chancroidal bubo treated by oral administration of sulphanilamide, and (iv) a mixed group.

In 11 cases of group 1, 6 successful results were obtained in 7 to 15 days. In group 2, after failing with the local application of a solution and of an ointment of sulphanilamide, Lepinay had 10 successes in 11 cases from the application to the sores of a very fine powder of sulphanilamide. In group 3 he had 5 successes in 8 cases, but he thought that sulphanilamide acted chiefly in cases in which a streptococcal or a staphylococcal infection was responsible. He recommended for chancroidal bubo combined treatment with dmelcos injections and oral administration of sulphanil-

amide. In group 4 it was noted that sulphanilamide did not affect the syphilitic element in a mixed chancroidal and syphilitic infection. 227

Lepinay (1938) considers that in chancroidal infection sulphanilamide acts chiefly on the streptococcal and staphylococcal infection rather than on the Ducrey bacillus, and that it is likely to succeed where dmelcos has failed.

Batchelor, R. C. L., and Lees, R. (1938) *Brit. med. J.*, **1**, 1100.
Hanschell, H. M. (1938) *Lancet*, **1**, 886.
Lepinay, M. (1938) *Bull. Soc. franç. Derm. Syph.*, **45**, 1728.
— (1939) *Maroc méd.*, No. 199, January.

CHILD GUIDANCE

TREATMENT

The number of Child Guidance Clinics in England has increased to more than 50 (see Vol. III, p. 131). 231

CHILD HEALTH AND WELFARE

See Surveys and Abstracts 1939, pp. 37 and 278. 232-234

CHOLERA

BACTERIOLOGY

The serological reactions of the true causal vibrio of cholera have been clarified by the work of Gardner and Venkatraman. The organisms were found to contain pure O heat-stable antigen obtained from saline-agar suspensions of smooth cultures boiled for 2 hours to remove the heat-labile H antigens. They were also non-haemolytic to goat's serum and constituted O subgroup I. O subgroups II to VI were mostly haemolytic and included paracholera, and cholera-like and some El tor vibrios, which are not specific organisms of cholera. The H antigen is also found in many non-choleraic vibrios, but not the O antigen subgroup I. Sera for the differentiation of the true organism should contain only the O antigen; those hitherto used contained H antigens and are unreliable. Bacteriological proof of cholera should therefore rest on the isolation of a non-haemolytic vibrio with the specific O antigen of subgroup I. 235

Gardner and White also found that all specific vibrios gave the type I Heiberg reaction of fermenting mannose and saccharose, but not arabinose. In addition, Taylor showed that they gave positive cholera red and negative Voges Prosauer reactions and that this combination of characteristics was not given by any of 558 non-agglutinable vibrios. Among the latter, Taylor *et al.* (1937) separated no less than 31 serological groups and 17 types by biochemical reactions, but found little or no evidence of their causal relation to cholera attacks. They concluded that vibrios of serological type differing from the true *Vibrio cholerae*, as above defined, did not produce cholera, nor was it likely that non-agglutinable types could develop into the typical agglutinable form. This was in agreement with prolonged investigations in cholera quarantine camps. The isolation of inagglutinable vibrios from cholera convalescents and healthy persons afforded no proof that they are ever the cause of the disease.

This important advance had also been confirmed in the field, for Taylor and Ahuja, working in 1938 in non-endemic cholera areas of the Punjab and the United Provinces, found in the water no vibrios agglutinating with group I O serum, such as have now been shown to be associated with typical cholera cases. The H agglutinating non-specific types in waters were therefore saprophytic. Moreover, in cholera cases in Assam, typical O agglutinating strains were almost invariably isolated, provided a large number of colonies were examined, and they all belonged to the biochemical Heiberg group I. It also followed that only smooth colonies, containing the specific immunizing heat-stable O antigen, should be used in preparing prophylactic vaccines. Taylor and Ahuja obtained identical serological and biochemical reactions with vibrios whose protein and carbohydrate fractions revealed 5 different types of chemical structure.

A report from Assam by Anderson threw doubt on the previously reported beneficial results in decreasing cholera by distribution of bacteriophage in water supplies.

235 **Pham found that small doses of cholera vibrio endotoxin, injected in the neighbourhood of the splanchnic nerve in rabbits and guinea-pigs, produced symptoms resembling those of cholera.**

PROGNOSIS

Turnbull confirmed the low mortality in the resistant Chinese, following the use of the hypertonic and alkaline salines intravenously. In an outbreak of cholera in South China, among hospital cases, which were of a severe type, the mortality in 400 to 500 cases was only 8 to 8·75 per cent.

TREATMENT

Anticholera inoculation. Taylor *et al* (1936) found that cholera vaccines would keep for 2 years in a hot climate. To produce effective immunity 5 to 6 days were required, but the immunity was higher after 8 to 10 days.

Ghosh immunized a horse against cholera toxins and reports that intraperitoneal injection of 70 to 80 c.cm. of the serum so obtained in 47 cases reduced the mortality to 10·63 per cent, against a mortality of 20·5 per cent in 170 controls. Further work is required on these lines.

Banerjee and Datta recommended sodium lactate in a dose of 10 c.cm. of a molar solution per kilogram of body weight in place of sodium bicarbonate intravenously.

Anderson, J. A. P., *King Edward VII Memorial Pasteur Institute, and Medical Research Institute, Assam. Report for 1936*, p. 7.
Banerjee, D. N., and Datta, S. K. (1936) *J. Indian med. Ass.*, **5**, 168.
Gardner, A. D., and Venkatraman, K. V. (1935) *J. Hyg., Camb.*, **35**, 262
and White, P. B. (1937) *Bull. Off. int. Hyg. publ.*, **29**, 1855.
Ghosh, H. (1936) *Brit. med. J.*, **1**, 936.
Pham, H. C. (1935) *C.R. Soc. Biol. Paris*, **119**, 78.
Taylor, J. (1937) *Bull. Off. int. Hyg. publ.*, **29**, 1843
and Ahuja, M. L. (1938) *Indian J. med. Res.*, **26**, 1
and Gurkirpal Singh, J. (1936) *Indian J. med. Res.*, **23**, 609
Pandit, S. R., and Read, W. D. B. (1937) *Indian J. med. Res.*, **24**, 931.
Turnbull, T. A. (1938) *J. R. nav. med. Serv.*, **24**, 138.

CHOREA

See also Surveys and Abstracts 1939, p. 278

DEFINITION

237 Although chorea should, in the present state of knowledge, be regarded as a form of rheumatism, because statistically 50 to 70 per cent of the cases show evidence of rheumatism at the time, or within 5 years of this attack, it cannot so easily be accepted that chorea, *per se*, suffices for the diagnosis of rheumatic activity, because the temperature and especially the sedimentation rate are usually normal in uncomplicated cases.

AETIOLOGY

Like all rheumatic conditions, chorea is prone to relapse, but, if the heart escapes damage in the first attack of chorea, it is more likely to remain unaffected in later attacks.

TREATMENT

Drugs. Sulphanilamide has been tried without success, the drug failing to produce any effect on the natural course of the disease.

Pyretotherapy. Some authorities have recommended treatment by artificial fever and have claimed remarkable results. The fever can be induced by typhoid vaccine or by electrotherapy. The protagonists of this method of treatment state that the chorea symptoms disappear quickly and that, although not causing any marked difference in the incidence of heart disease, it seems to help by modifying the severity of the cardiac lesions. Others agree to the definite symptomatic improvement that might follow these measures, but are not convinced that they are of any real and lasting value.

In a report authorized by the Council on Physical Therapy of the American Medical Association, however, Krusen and Elkins recommend the further use of physically-induced fever in the treatment of chorea. It is claimed that fever therapy inhibits choreiform movements in 80 per cent of cases, lowers the incidence of rheumatic manifestations, and cuts short the choreic attack. A course of 10 or 12 sessions of between 2 and 3 hours daily, at which the body temperature is maintained at 104 to 105° F. (40 to 40·5° C.) is recommended. The authors consider that physical methods are preferable to typhoid vaccine in inducing fever. 237

Krusen, F. H., and Elkins, I. C. (1939) *J. Amer. med. Ass.*, **112**, 1689.

CHOREA, HUNTINGTON'S

See Surveys and Abstracts 1939, p. 279. 238

CLIMACTERIC AND ITS DISORDERS

See also Surveys and Abstracts 1939, p. 279

THE QUESTION OF A CLIMACTERIC IN THE MALE

Treatment

Hormone therapy.—Recently Miller *et al.* reported the treatment with testosterone propionate of 6 men, 2 of whom were adult castrates, 2 had hypogonadism, and 2 apparently had psychic impotence. The dosage varied from 20 mg. daily or 3 times weekly and was carefully controlled by injections of appropriate series of the oily solvent only. In addition to markedly diminished libido and inadequate erections, these patients, prior to treatment with testosterone, were disturbed, anxious, and broken in spirit. They varied from moderate to severe states of mental depression. The 4 cases with definitely organic lesions displayed additional symptoms such as vasomotor disturbances, very definite emotional instability characterized by sudden uncontrollable changes in mood, tendency to cry, irritability and, sometimes, sullen anger. Adequate treatment with testosterone propionate produced remarkable clinical improvement, characterized by marked increase in erectile capacity and sensitivity of the penis, in libido, and in the capacity to respond with the proper emotions not only to intercourse but also to other acts, such as kissing and embracing. The 2 castrates, during treatment, appeared to be restored to normal in these respects. Normal sex functions and motivation were accompanied by great changes in the entire mental attitude of all patients. 243

Werner describes cases treated by him with testosterone propionate. The first was a man of 50, passing through the climacteric, and exhibiting the typical symptoms; he was given 10 mg. of testosterone propionate in oil intramuscularly 3 times a week. After 4 weeks his subjective symptoms had markedly improved, his depression had gone, and he felt cheerful. After 3 months the symptoms had entirely disappeared, but they began to return after discontinuance of treatment.

In another case of a unilateral castrate with atrophy of the remaining testis and complaining of similar symptoms with loss of sex function, 10 mg. of testosterone propionate in oil were given 3 times a week during the first month, twice a week during the second month, and once a week during the third month. After the third injection he had an erection and coitus with an orgasm; he had not had an erection for 9 months previously. During the first month he had 3 to 4 erections a week, but on the smaller dosage of the second month he had only one erection a week. It required 3 injections weekly to maintain him at normal. It is thus apparent that testosterone can relieve the symptoms of an artificial or natural climacteric in men and can restore the function of the erectile tissue in the sex organs.

Miller, N. F., Hubert, G., and Hamilton, J. B. (1938) *Proc. Soc. exp. Biol., N.Y.*, **38**, 538.
Werner, A. A. (1939) *J. Amer. med. Ass.*, **112**, 1441.

CLIMATE IN THE TREATMENT OF DISEASE

See Surveys and Abstracts 1939, p. 280. 244

CLONORCHIASIS

PARASITOLOGY

245 H. Kawana reported that, in the district of Shanghai, dogs, cats, and rats had been found to be reservoir hosts for *Clonorchis*. Of 15 house dogs, none was infected, but of 228 'field' dogs 36·6 per cent were infected; 58 per cent of 202 cats were infected. The fish *Hypomedus olidus* had been found by Ide to act as host for the larval stage of *C. sinensis*. This fish being eaten raw was therefore dangerous. It is the first member of the Salmonidae to be incriminated.

Treatment

Kawai administered gentian violet orally to 7 dogs infected with *C. sinensis* and estimated the results by egg counts. He confirmed the efficacy of this drug, especially for light infections, in which the worms were reduced by 61 per cent in 15 days. The dose varied in light cases 18 mg. per kilo body weight once every 3 days for 15 days to a total dose of 1,200 mg.; in a moderate case of 18 to 20 mg. per kilo body weight daily for 19 days to a total dose of 3,040 mg., and in a heavy infection 120 mg. (10 to 12 mg. per kilo body weight) daily for 45 days, to a total dose of 5,400 mg.

TREATMENT

Gentian Violet

Erratum

Vol. III, p. 225, para. 7, line 6, after '300 mgm.' insert 'per kilogram of body weight'.

Ide, K. (1936) *Kitasato Arch.*, **13**, 40
Kawai, T. (1937) *J. med. Ass. Formosa*, **36**, 386
Kawana, H. (1936) *J. Shanghai Sci. Inst.*, **2**, 75.

COCCYX DISEASES

246 See Surveys and Abstracts 1939, p. 281

COELIAC DISEASE

See also Surveys and Abstracts 1939, p. 282

AETIOLOGY

247 There is considerable controversy about the impairment of absorption of various food factors, particularly carbohydrate and vitamins, in coeliac disease. The malabsorption of carbohydrate might be secondary to the intestinal hurry and general impoverished absorption from debility. Some, however, consider that it is a part of the disease. Parsons pointed out the liability of patients on a low-fat diet to suffer from deficiency of the fat-soluble vitamins and always included large doses of antirachitic substances in the diet (e.g. irradiated ergosterol dissolved in paraffin or in powder form (calciferol)). Parsons, in conjunction with Wallace Ross, investigated the blood-sugar curves in coeliac disease by means of oral and intravenous glucose-tolerance tests, and also the insulin sensitivity, and concluded that poor absorption of carbohydrate rather than endocrine dysfunction was responsible for the flat and low blood sugar curves, and after testing Himsworth's hypothesis, namely, that insulin was activated by an 'insulin kinase' produced chiefly in the liver, agreed that there might be a deficiency of this substance also.

TREATMENT

Following the investigations reported above Parsons and Wallace Ross administered liver preparations (campolon), and found that, particularly when these substances were given by mouth, the intravenous glucose-tolerance curves became more normal. Parsons also recommended the administration of vitamin B_2; this was based upon Verzar's observation that fat, glucose, galactose, and vitamin B_2 (lactoflavin) were all absorbed from the intestine by a process involving transfer of phosphoric acid from one compound to another (phosphorylation). Interference with this process would be expected to diminish absorption of vitamin B_2.

Parsons, L. G. (1938) *Brit. med. J.*, **2**, 929.

COLDS

See Surveys and Abstracts 1939, p. 283. 248

COLIFORM BACILLUS INFECTIONS

See also Surveys and Abstracts 1939, p. 285.

TREATMENT

Recent investigations on coliform bacillus infections have centred round the use of drugs of the sulphonamide group. By a course of treatment with sulphanilamide lasting one or 2 weeks the urine can be sterilized. But a few months after cessation of treatment, *Bact. coli* often reappear in the urine, especially in cases in which the male genital organs have become involved. There is as yet no conclusive evidence that this drug is superior to mandelic acid, or that it is as effective against *Bact. coli* infections as it is against the coccal group of organisms. 249

COLITIS

See Surveys and Abstracts 1939, p. 286. 250

COLON, CARCINOMA OF

See Surveys and Abstracts 1939, p. 288. 251

CONCUSSION AND COMPRESSION

See also Surveys and Abstracts 1939, p. 289 255

TREATMENT

Of Contusion

Erratum

In Volume III, p. 362, 4 lines from foot of page, the strength of magnesium sulphate solution for use per rectum stated as '(3 grains in 6 ounces of warm water)' should read '(3 ounces in 6 fluid ounces of warm water)'.

CONJUNCTIVA, INJURIES AND DISEASES

See also Surveys and Abstracts 1939, pp. 128 and 289.

INCLUSION CONJUNCTIVITIS

Treatment

Sulphanilamide.—The average time for healing of inclusion conjunctivitis has been about 6 months, but some cases have lasted for over a year. P. Thygeson tried sulphanilamide in the experimental disease in 2 rhesus monkeys, and found that a daily dosage of 0·5 gr. per pound body weight resulted in complete healing of the disease in 2 weeks. In 2 control animals there was no change during this period. This experiment led the author to employ sulphanilamide in a woman, aged 34, with an acute unilateral conjunctivitis of 2 weeks' duration, and characterized by follicular and papillary hypertrophy most marked in the conjunctiva of the lower lid. There were swelling of the pre-auricular gland, pseudoptosis and bulbar injection with oedema of the limbus, but no epithelial or corneal changes. No significant bacteria were discovered by cultures and scrapings, but moderate numbers of epithelial-celled cytoplasmic inclusion bodies characteristic of inclusion conjunctivitis were observed. Sulphanilamide, in a dosage of 10 gr. 3 times a day with equal quantities of sodium bicarbonate, was given daily, and no local treatment was employed. On the second day the bulbar injection and conjunctival secretion began to diminish. This improvement continued steadily and, 13 days after the beginning of treatment, the eye had returned to normal, except for the presence of a tiny island of follicular hypertrophy in the outer part of the lower fornix. Since a similar island of hypertrophy existed in the other eye, this condition may well have 256

256 preceded the infection. Sulphanilamide was stopped at the end of 21 days, and 2 months later there was no evidence of recurrence. After the second day of treatment inclusion bodies could not be found in the slides.

Thygeson, P. (1939) *Amer. J. Ophthal.*, **22**, 179.

CONSTIPATION

257 See Surveys and Abstracts 1939, p. 50.

CONTRACEPTION

METHODS OF CONTRACEPTION

Spermicidal Preparations

258 *Summary.* Extensive research for the improvement of spermicidal substances undertaken under the auspices of the Birth Control Investigation Committee has led to the standardization of laboratory tests for spermicidal efficiency and for harmlessness. Baker and his co-workers discovered that phenylmercuric acetate and phenylmercuric nitrate were the most spermicidal substances known, being 512 times as spermicidal as quinine bisulphate and chinosol, and effective in acid and alkaline media. The acetate is now marketed in the form of paste and gels under the names volpar paste and volpar gel. These laboratory results, however, have yet to be confirmed by clinical trials, which are proceeding.

Baker, J. R., Ranson, R. M., and Tynen, J. (1938) *Lancet*, 2, 882.

CONVULSIONS IN INFANCY AND CHILDHOOD

259 See Surveys and Abstracts 1939, p. 291.

CORNEA, INJURIES AND DISEASES

See also Surveys and Abstracts 1939, pp. 131 and 292.

ULCERS

Treatment

260 The instillation of prontosil has been found to be remarkably effective in the treatment of inflammation of the cornea. In cases in which ulceration has occurred, its use has given rise to rapid healing. Prontosil causes no irritation of the conjunctiva, and appears to have a direct bactericidal effect, causing rapid disappearance, generally in 3 days, of the causal organism, particularly when this is the gonococcus or the staphylococcus. Saline irrigations may be used in conjunction.

Pellman Glover, L. (1939) *Amer. J. Ophthal.*, **22**, 179.

CORNS AND BUNIONS

261-263 See Surveys and Abstracts 1939, p. 294.

CORONERS AND INQUESTS

NOTICE OF DEATH

264 What is a natural death? The criterion proposed for deciding whether a death is natural, namely, "Have I any reason to suspect that death is not a natural one?" requires amplification by consideration of some border-line cases between natural and unnatural deaths. Heat and cold deaths are in general natural; a weak heart may not be able to stand the extremes of even the temperate English climate and must therefore be regarded as a heart death, but a person with a healthy heart will succumb if shut up in a refrigerator or an incubator, such deaths would be unnatural. Death from inhalation of food is also natural; the moribund person vomits and inhales food because he is dying, and does not die because he has inhaled food, as witness the absence of any reaction in the air passages. Bathroom deaths on the

other hand are usually unnatural. The explanation is often given that a good meal plus the heat of bath and bathroom were too much for the victim; but none of these conditions will affect a healthy heart. Rarely the patient is said to be the subject of lymphatism, but more often he is suffering from carbon monoxide or nitric oxide poisoning. If a geyser is used without a baffler and without proper ventilation, the atmosphere of the bathroom soon becomes poisonous; moreover, it must be remembered that besides carbon monoxide, which kills fairly slowly, nitric oxide must also be reckoned with. Coal gas contains acetylene which, burned in a confined space, produces nitric oxide, which is very poisonous and acts quickly. 264

What is violence? An operation is, technically, an injury, and a death which is the direct consequence of it must be reported. Medical practitioners are not in the habit of regarding an operation as trauma, and they are encouraged in this view by the administrative requirement that 'death following operations necessitated by injury' must be reported. Obviously they must, and so must all deaths associated with operations, if it is thought that the operation has any causal connexion with the death. On the other hand, if the patient's condition would have been fatal had there not been an operation - as for example in strangulated hernia, diphtheritic asphyxia, or ectopic gestation - and the patient dies during or after the operation, the coroner may, on suitable advice, consider that the effect of the operation and the anaesthetic were negligible in comparison. Many know that an operation death must be reported, but think that it is necessary only when it occurs on the operating table, or within 24 hours after the operation. This is unsound; a death occurring even weeks after should be reported, if it is thought that the operation was responsible. This confusion arises from the rule of some hospitals that all deaths occurring within 24 hours of operation, or of admission, must be reported; this, however convenient to the hospital, is at times puzzling to the coroner.

Anaesthetic deaths are deaths from suspected poisoning, and are reportable. Usually there is some idiosyncrasy, or an unexpected gross lesion, as when chloroform kills a man with a fatty heart. A distinction must, however, be made between deaths from an anaesthetic and deaths occurring while the patient is under an anaesthetic. Surgical shock accounts for a good many so-called anaesthetic deaths. In some cases neither need be invoked as the patient dies from the disease for which he is being operated on (e.g. toxaemia from strangulated hernia). Ether at times even prolongs life.

As regards alcoholism: it may be added that it is unfair and absurd to sign up a case as alcoholism merely because cirrhosis of the liver is present, cirrhosis of the liver is also found in children and horses.

Erratum

Page 439, line 12. For 'accident' read 'trauma'.

Addendum

Page 439, line 22, add: It is in general useless to ask the coroner (say by telephone) if it is permissible to give a certificate, since the moment the practitioner communicates with him he is put on inquiry, and must send his officer to obtain particulars.

CRANIAL NERVE AFFECTIONS

See Surveys and Abstracts 1939, pp. 86 and 294. 267-274

CROHN'S DISEASE

See also Surveys and Abstracts 1939, pp. 49 and 294. 277

AETIOLOGY

Crohn has reviewed the subject of Crohn's disease (regional ileitis), basing his conclusions on 110 patients observed by him in about 8 years. The ratio of males to females was 3:2. The aetiology was still unknown, but he favoured the hypothesis of an infective agent.

MORBID ANATOMY

Hurst has enumerated the cases previously recorded in England and described 3 more, in 2 of which fistulae developed, this being the first record of this complica-

277 tion in England. In the first patient, a woman aged 27, there were fistulous communications joining the small intestine with other parts of the small intestine, the transverse colon, and the pelvic colon—at least 7 holes being present. A difficult and complicated operation was performed, and 6 months later the patient was free from symptoms. In the second case, that of a woman aged 74, the radiograph after a barium sulphate meal indicated the presence of fistulae, one from the small intestine into the extraperitoneal tissues, and an abscess cavity in the pelvis. Operation was not possible, but at the time of writing, nearly 2 years after this examination, the patient was living a normal life, though she complained of occasional pain.

Bowen and Day described the histological changes in a woman who came to necropsy (death being due to a uterine tumour) 9 years after ileo-colostomy performed for Crohn's disease. They reported that the mesentery, except in the immediate neighbourhood of the affected intestine, was normal, and considered that this supported the view that the involvement of the mesenteric lymphatic apparatus was secondary to the lesions in the ileum rather than the cause of them.

CLINICAL PICTURE

In Crohn's series of cases the onset was acute in 11, but symptoms had been present for 1 to 5 years in 62 patients, for 5 to 10 years in 15, and for more than 15 years in 8. Signs of obstruction were present in 10 cases only. The tendency to form fistulae was marked: internal fistulae were present in 11 cases, external (opening into a laparotomy scar) in 12, and peri-anal, rectal, and recto-vaginal in 20 (some of the tracks were long and circuitous). The prognosis in acute cases varied; some cases appeared to undergo spontaneous cure without resection. Spontaneous regression was not observed in chronic cases.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Hurst pointed out the importance in doubtful cases of occult blood in the stools. In recurrent subacute appendicitis, the condition most often confused with it, occult blood was rare, whereas, in his 7 cases of Crohn's disease, it was present in all.

Hurst also discussed the possibility that, in the past, cases of Crohn's disease had escaped recognition, and commented on 2 cases diagnosed as tuberculous enteritis, one in 1923 and the other in 1925, but which he diagnosed in retrospect as Crohn's disease. He suggested that in doubtful cases inflation of the ileum with air through the colon might be useful in excluding Crohn's disease, in a boy, aged 14, at first diagnosed as Crohn's disease, this method showed that the condition of the intestine was normal, the great resulting distension of the ileum excluding the existence of terminal ileitis.

TREATMENT

Medical treatment should be restricted to patients in whom operation is impossible owing to the extensive involvement of the intestine. Surgically a higher percentage of permanent cures is obtained from resection than from short-circuiting operations. Among 39 resections there were 3 recurrences, probably owing to the difficulty of recognizing at operation the upper limit of the affected mucosa; this was rendered more difficult by the fact that the inflammatory process is not always continuous, but may be interrupted by one or more 'skip areas', extending as far as 18 inches.

Bowen, W. H., and Day, T. D. (1939) *Guy's Hosp. Rep.*, **89**, 70.
Crohn, B. B. (1939) *Surg. Gynec. Obstet.*, **68**, 314.
Edwards, H., and Hurst, A. (1939) *Guy's Hosp. Rep.*, **89**, 76.
Gill, W. G. (1939) *Guy's Hosp. Rep.*, **89**, 77.
Hurst, A. (1939) *Guy's Hosp. Rep.*, **89**, 54, 66, 79, 80.

CYANOSIS, ENTEROGENOUS

See also Surveys and Abstracts 1939, pp. 176 and 295

Aetiology

279 *Sulphonamide drugs.*—Sulphaemoglobinaemia and methaemoglobinaemia readily occur as the result of treatment with any of the sulphonamide drugs, because these drugs catalyse the reaction between sulphuretted hydrogen and haemoglobin. No

deaths have been recorded, and the cyanosis is not considered to be sufficient cause for ceasing this treatment when it is urgently required. Putrefaction, with the formation of sulphuretted hydrogen, occurs when the colon is full of fluid. When sulphonamide drugs are being taken, therefore, saline purges and drastic purges should be avoided, and sulphur-containing foods should be prohibited. Liquid paraffin is the safest laxative. 279

Treatment

The methaemoglobinaemia caused by sulphonamide drugs may be treated by the intravenous injection of methylene blue (0·1 to 0·2 c.cm. per kilogram body weight of a 1 per cent aqueous solution) or by the administration of 0·5 to 1·0 g. per day of methylene blue by the mouth (Wendel, 1939).

Wendel, W. B. (1939) *J. clin. Invest.*, **18**, 179.

DARIER'S DISEASE

MORBID ANATOMY

Senear confirmed the presence of the typical 'round bodies' in the warty growths as well as in the follicular lesions and commented on the hitherto unobserved phenomenon of seasonal variation. 282

TREATMENT

Dittrich recorded a 'cure' with intramuscular injections of solganol B oleosum in a case which had lasted for 16 years. Stoltz, from an experience of 4 cases, recommended treatment with Grenz rays (2 applications of 1200 *r* at intervals of 3 months).

Dittrich, O. (1936) *Derm. Z.*, **74**, 207.
Senear, F. S. (1938) *Arch. Derm. Syph.*, **1**, 705.
Stoltz, F. (1937) *Derm. Wschr.*, **105**, 1266

DEAF-MUTISM

AETIOLOGY

According to Hallpike deaf-mutism is not infrequently due to trauma, he described in detail the histological changes in the temporal bones and internal ear of a man who died at the age of 59, and had been regarded as a deaf-mute and said to have been 'always' deaf, though the deafness was only established with certainty at the age of 3. Histologically there was an unhealed transverse fracture of the labyrinth capsule on the right side; this threw some doubt on the arguments of others that changes described by them, and indistinguishable from those in the present case, were the result of congenital malformations or developmental failure. Birth injury or trauma in early life must have been responsible for the lesion in this case. 283

Hallpike, C. S. (1937), *J. Laryng.*, **52**, 661.

DEAFNESS

See also Surveys and Abstracts 1939, pp. 100 and 296.

DIAGNOSIS

Nerve Deafness

Causes

Watkyn-Thomas reviewed the present outlook on internal-ear deafness in a discussion at the Royal Society of Medicine (1938). He enumerated the causes and assigned importance to the possibility of production of changes in the endolymph by toxins, either blood-borne or originating in the middle ear, especially in cases characterized by an abrupt fall in the perception of high tones, starting soon after the age of 40. Special attention was directed to the damage known to be caused to the ear by quinine, and it was pointed out that salicylates, arsenic, petroleum benzine vapour, and tobacco might all cause internal-ear deafness. The elimination of septic foci was advocated, dental sepsis being the most important; tonsillar sepsis 284

284 was also a factor, but the accessory sinuses apparently not. Intestinal lavage occasionally improved the ear condition, but investigation particularly of the appendix, gall-bladder, and prostate was recommended. It had also been proved by various workers that long-continued noise could damage the organ of Corti. Reference was made to the work of Crowe, Guild, and Polvogt, who confirmed the view that the receptors for high tones are situated in the basal turn of the cochlea.

TREATMENT

Otosclerosis. In a discussion at the Royal Society of Medicine (1936), eleven speakers presented their results from the treatment of otosclerosis by the intratympanic injection of thyroxine, according to the method of Albert Gray. It was generally felt that the results were uncertain and that the treatment did not fulfil the hopes originally raised.

Discussion on intratympanic medication, with special reference to thyroxine, *Proc. R. Soc. Med.* (1936) **29**, 1691.
Watkyn-Thomas, T. W. (1938) *Proc. R. Soc. Med.*, **32**, 487.

DEATH, SUDDEN AND UNEXPECTED

285 See Surveys and Abstracts 1939, p. 298.

DENTAL SEPSIS IN RELATION TO SYSTEMIC DISEASE

See also Surveys and Abstracts 1939, p. 298

CONDITIONS ASSOCIATED WITH DENTAL SEPSIS

Subacute Bacterial Carditis

288 S. D. Elliott has again called attention to the occurrence of transient streptococcal bacteriaemia as a sequel to dental extraction. Acute apical infections are not so commonly the source of such an invasion as parodontal infections. Chronic gum infection is especially likely to cause bacteriaemia even apart from dental operations, this may result from slight trauma, such as mastication of hard food, brushing the gums, or 'rocking' a tooth. Although this bacteriaemia usually produces no remote ill effects, Elliott considers that subacute bacterial endocarditis may result in patients with pre-existing valvular deformity, either congenital or rheumatic. Elliott reports that, of 56 patients with bacterial endocarditis, 13 dated the onset of their illness from a dental operation. 9 of these 13 were admitted to hospital with fully developed bacterial endocarditis within 8 weeks of the operation, and the others within 6 months. Elliott considers that in patients with any cardiac abnormality scrupulous care should be taken when dental extractions are essential, and 'rocking' a tooth before extraction should especially be avoided.

Dyspepsia and Rheumatism

J. M. Vazey and A. F. Clark-Kennedy have reviewed the relation between dental sepsis and general diseases (anaemia, dyspepsia, and rheumatism). As a result of increased knowledge of the aetiology of anaemia, dental sepsis is no longer regarded as an aetiological factor. As regards dyspepsia, the authors' observations suggest that the loss of the power of proper mastication is a potent cause of dyspepsia, particularly during the period after the teeth have been extracted and the dentures not yet fitted. Of 76 dyspeptic patients from whom the teeth were removed, 6 were benefited, of 126 patients from whom the teeth were extracted for dental reasons, 39 (31 per cent) developed dyspeptic symptoms. The authors consider that the aetiological importance of dental sepsis in rheumatism is equally uncertain. Of the 126 patients whose teeth were removed for dental reasons, 19 (15 per cent) developed rheumatic symptoms.

DIATHERMY IN DENTISTRY

S. Garbarska-Sarcina reports on the use of diathermy for 'devitalizing' the pulp of a tooth, i.e. for filling the pulp tissue and for destroying or inhibiting the action of bacteria. The method is important in the treatment of focal infections, which generally arise from decomposed pulp tissue. Because of the coagulation of the tissue produced by the current, haemorrhages cannot occur. Diathermy also

augments the action of drugs; the effect of chloramine and hypochlorites is increased about 20 times when the temperature is raised by 20 to 50° F. 288

Elliott, S. D. (1939) *Proc. R. Soc. Med.*, **32**, 747.
Gabarska-Sarcina, S. (1939) *Brit. J. phys. Med.*, N.S. **2**, 130.
Vaizey, J. M., and Clark-Kennedy, A. E. (1939) *Brit. med. J.*, **1**, 1269.

DENTITION

See Surveys and Abstracts 1939, p. 299. 289

DERMATITIS DUE TO INJURY AND POISONING INCLUDING FEIGNED ERUPTIONS

See Surveys and Abstracts 1939, p. 299. 290

DERMATITIS HERPETIFORMIS

See Surveys and Abstracts 1939, p. 300. 292

DESMOID TUMOURS

Morbid anatomy.—Under the title 'dermoid sarcoma of the rectus abdominis' Dodd reported a tumour, provisionally diagnosed as a dermoid tumour in the rectus, in 1931 it was removed and reported as microscopically a fibrosarcoma infiltrating muscle. It recurred a year later and was widely removed, and was reported on similarly. It has not recurred or been followed by noticeable bulging or weakness of the abdominal wall. 294

Dodd, H. (1939) *Post Grad. med. J.*, **15**, 96.

DIABETES INSIPIDUS

See also Surveys and Abstracts 1939, p. 301.

TREATMENT

Von Matolay treated 9 patients with diabetes insipidus by transplantation of a calf's pituitary between the sheath of the rectus abdominis and the peritoneum. In 2 patients the operation was repeated once, and in one patient twice, making a total of 13 operations. The ages of the patients ranged from 4½ to 31 years. Six operations resulted in temporary improvement, lasting a few days, and the other 7 produced a more lasting improvement—up to 10 months. The author considers that, for patients who are resistant to hormone therapy, the remission of symptoms even for a few months by this method is of great benefit. The method appears to be without danger. 295

Experiments on dogs and cats have indicated that polyuria caused by injury to the pituitary or hypothalamus was abolished by thyroidectomy and re-established by administering thyroid. Following this indication, Findley performed a thyroidectomy on a man aged 55 suffering from polydipsia and polyuria of one year's duration. His basal metabolic rate prior to operation was −16 per cent., after operation it fell to between −35 and −40 per cent. The operation did not seem to have a greater diuretic effect than a low-salt diet. Findley considers that the diuretic action of thyroid is not due to its stimulating action on metabolism, for when the patient's basal metabolism was raised to the pre-operative level by dinitrophenol there was no increase in urinary output, whereas when it was raised by administration of thyroid there was an increase in the volume of the urine.

The patient felt somewhat better after the operation, showed an increased response to pitressin, and was more tolerant to salt than before the operation, but the author is not in favour of repeating the procedure. In this patient it was noticed that, in the pre-operative period, salyrgan (mersalyl) increased the output of chloride in the urine as in normal individuals, indicating that, if diabetes insipidus is due to inability of the kidneys to void urine, the defect is not irremediable.

Findley, T. (1937) *Ann. intern. Med.*, **11**, 701.
Matolay, G. von (1938) *Arch. klin. Chir.*, **191**, 73.

DIABETES MELLITUS

296 See Surveys and Abstracts 1939, pp. 67 and 301.

DIAPHRAGM DISEASES

297-304 See Surveys and Abstracts 1939, p. 309.

Vol. IV

DIARRHOEA

ALTIOLOGY AND PATHOLOGY

Diarrhoea due to Hyperthyroidism

305 It is now recognized that diarrhoea may be the presenting symptom in mild hyperthyroidism. It generally stops as soon as iodine is administered or, in more severe cases, after thyroidectomy.

DIARRHOEA ASSOCIATED WITH FLAGELLATE INFECTION

306 See Surveys and Abstracts 1939, p. 310.

DIARRHOEA IN INFANCY AND CHILDHOOD

308 See Surveys and Abstracts 1939, p. 310.

DIATHERMY

INDICATIONS

Superfluous Hairs

309 The technique of Hopfinger, which is a definite improvement on the direct current method of removing superfluous hairs, has now become available in Great Britain. It is carried out by diathermy, and it is essential to have a finely balanced needle holder and a smoothly working switch in the holder. An accurate replica of Hopfinger's pattern is now manufactured in this country. The type of needle is also important. It must be a No. 14 pearl threading needle; it is coated, except the 2 mm. near the point and 1 cm. at the eye end, with a special insulating lacquer also made by Hawkins. The needle is passed in the follicle directly to the bulb of the hair and the current strength should be such that the patient feels a very slight sensation of discomfort for about one-fifth of a second. The current should be so adjusted that not more than 2 such short contacts, preferably one, enable the hair to be withdrawn without any resistance and with a black end at its root. There should not be any sign of superficial whitening of the skin. With practice, this technique can be carried out at the rate of 4 to 6 hairs per minute and without leaving scars and practically without subsequent induration. The same technique can be applied with great benefit to cases of acne pustuliformis. After each sebaceous cyst has been evacuated by pressure with a metal spatula pierced with a hole, the needle is passed into the sebaceous cyst and the same technique is carried out in each evacuated pustule.

DIET IN TREATMENT

310, 311 See Surveys and Abstracts 1939, p. 311.

DIETETIC DEFICIENCY DISEASES

312-323 See Surveys and Abstracts 1939, p. 311.

DIPHTHERIA

See also Surveys and Abstracts 1939, pp. 41 and 312.

ALTIOLOGY

324 The incidence of diphtheria in Europe appears to be increasing, according to the report of the Health Section of the League of Nations. This is disturbing because

diphtheria is a preventable disease. In Canada the incidence of, and mortality from, diphtheria has been greatly reduced by immunization of the population (Fitzgerald *et al.*), and 3 doses of toxoid produced an immunity as high as that in natural immunes and reduced the incidence among those so vaccinated by 90 per cent. In Toronto the morbidity rate from diphtheria fell from 164 per 100,000 in 1930 to 3·5 in 1934. Between January 1934 and March 1935, and also during 1937, no death from diphtheria was recorded in Toronto. 324

DIAGNOSIS

The use of the Solé or Folger-Solé swab is still favourably reported on. Recently, however, Manzullo of Buenos Aires advocated a rapid method of diagnosis. A 2 per cent solution of potassium tellurite was prepared by dissolving the salt in distilled water at 40° C. A swab dipped in this solution was then made to touch the membrane or exudate. The presence of *C. diphtheriae* will cause blackening of the swab in 5 to 10 minutes. Care must be taken to avoid contact with the tongue, as its mucous membrane also has the power of blackening the swab. The value of this test has been seriously questioned by others (see Surveys and Abstracts 1939, p. 312).

TREATMENT

Prevention

Immunization.— In assessing the results of Schick tests, it is no longer believed that $\frac{1}{50}$ unit of antitoxin per c.cm. of blood is necessary to give a negative result; Parish and Wright found that a negative result might be given by persons whose immunity was insufficient to withstand virulent gravis or intermediate strains; a negative response might be given to fourfold toxin with only 0·002 to 0·005 unit of antitoxin per c.cm. and to tenfold toxin with only 0·01 to 0·002 unit. As regards choice of prophylactic, present indications are that alum-precipitated toxoid will be the prophylactic of the future. Chesney starts by injecting a 'detector' dose of 0·2 c.cm. (0·1 c.cm. in children over 10); this is followed after 4 weeks by 0·4 c.cm. of A.P.T., unless the 'detector' dose has elicited sensitivity, in which event the second dose is reduced. The 'one-shot' method of prophylaxis was no longer recommended; at least 2 injections should be made at intervals of not less than 2 weeks. The preparation of concentrated antitoxin containing 6,000 or more units per c.cm., obtained by pepsin digestion of the proteins, was an important advance. Serum sickness after the use of these 'globulin-modified' antitoxins has been reduced to negligible proportions.

Fitzgerald, J. G., Fraser, D. T., McKinnon, N. E., and Ross, M. A. (1938) *Lancet*, **1**, 391.
Harries, E. H. R. (1939) *Lancet*, **1**, 45.
Health Section of League of Nations Report (1938) *Brit. med. J.*, **2**, 1242.
Manzullo, A. (1938) *Folia Biol.*, 366 (Reported in *Lancet*, **2**, 1181, 1938).
Parish, J. H., and Wright, J. (1938) *Lancet*, **1**, 882.

DISLOCATIONS, FRACTURES, FRACTURE-DISLOCATIONS, AND ASSOCIATED INJURIES

See also Surveys and Abstracts 1939, p. 314.

REGIONAL

Shoulder Joint

In fractures of the great tuberosity of the humerus without gross displacement, immobilization in abduction is rather liable to lead to a stiff shoulder, and it is for this type of case that relaxed circumduction from the first day gives the best results. The patient is shown how to bend over sideways with his arm hanging away from his body and, by general pendulum swinging of the arm, describe a circle with his hand, which gradually increases in circumference as pain and spasm disappear. It appears that the broken-off fragment of the great tuberosity does not become displaced by this manœuvre, because it is performed with all the shoulder muscles relaxed, the weight of the arm being used to give the necessary distraction. 328

Rupture of Supraspinatus Tendon

331 A fair number of the complete tears are still missed, mainly because they are not suspected, and surgeons are rather unwilling to explore the doubtful cases. The condition is still a new entity to most of the medical profession and, as such, is worthy of emphasis. The diagnosis of complete rupture is made as follows. (i) The patient is unable to abduct the humerus to a right angle, in spite of the strongly-acting deltoid. (ii) When the humerus is abducted passively to a right angle the patient can hold it there, but when asked to lower it there is a click which can be felt as the head shifts from its pivoting point in the glenoid cavity and slips upward, the arm at the same time dropping suddenly to the side of the body. The patient cannot lower the arm gradually. (iii) There is always tenderness over the great tuberosity of the humerus, and there is sometimes referred pain over the insertion of the deltoid. (iv) Radiographs are negative.

In cases of inflammation of the supraspinatus tendon with calcification, aspiration under local anaesthesia and washing out the subdeltoid bursa with physiological saline through 2 needles give immediate relief, but may have to be repeated. The results of this treatment are quite dramatic.

Elbow Joint

Internal Epicondylar Separations

333 Even when the internal epicondyle is separated and pulled into the joint, manipulation by abduction of the forearm on the arm and pull on the flexor origins may be successful in reducing it. Radiographic confirmation of reduction is necessary. In such a case the only indication for operation would be non-recovery of the bruised ulnar nerve. Pegging back or excision of the epicondyle is by no means always necessary in order to obtain a good functional result.

As regards injuries and fractures of the elbow joint, emphasis must be laid on the importance of the use of active movements only and on absolute avoidance of passively stretching the fibrous tissue, as the latter further aggravates the disability and may set up myositis ossificans.

Wrist Joint

Fractured Scaphoid

335 In fractures of the scaphoid with no displacement the plaster should be applied as follows: the hand is put in radial deviation and the thumb in opposition, and the plaster should extend distally to hold the first metacarpal, the proximal half of the proximal phalanx should, therefore, be included, otherwise the distal fragment of the scaphoid is likely to have some range of movement.

Hand

Bennett's Fracture

336 Better reduction and maintenance of position in this fracture can be achieved by a steel pin through the pulp of the thumb, and elastic traction with a piece of rubber tubing attached to an extension bow formed by strong wire incorporated in a plaster cuff round the forearm.

Mallet Finger

A neat plaster splint may be made for a mallet finger by making a tube of dry plaster-of-Paris bandage, putting the finger into it, and pressing the finger and thumb together in such a way as to hyperextend the affected finger, then immersing the whole hand in water and moulding the plaster neatly to fit the finger. This should be left on for 6 weeks.

Pelvis

337 In a fracture separation of the symphysis pubis, or other fracture in which the pelvic ring is opened up, remarkably good reduction of the fracture may be achieved by nursing the patient mainly on his sound side instead of on his back, for this position opens up the pelvic girdle.

Fractures of Femur

339 Well-leg traction has proved a great advance in the treatment of this type of case but requires very careful padding and application of plaster; particular care must be taken in the padding and the fitting of the plaster on the sole of the foot on the undamaged side (Anderson).

Mid-Shaft Fractures of the Femur 339

The Hamilton Russell method of extension, consisting of a canvas sling under the knee, stretching extension on the lower leg, and a movable pulley attached to the lower leg extension and only 8 lb. of traction, facilitates very comfortable nursing. It does away with the necessity for a pin or a wire through the bone. The materials required are easily improvised. The use of this method is largely justified by practice in America and in England (Hamilton Russell).

Knee Joint

Fracture of the Patella

Excision should still be reserved for cases with special indications such as comminuted fracture, compound fracture, and failed suture. The usual transversely-fractured patella is still best treated by conventional methods. 340

Complications of Spinal Fractures

Paraplegia

Interference with bladder function always involves a decision whether the bladder should be drained suprapubically, by tied-in catheter, or by repeated catheterization. The bladder receives sympathetic supply from the first and second lumbar cord segments; this relaxes the detrusor and closes the sphincter. The parasympathetic supply from the second and third sacral segments causes contraction of the detrusor and relaxation of the sphincter. If, therefore, the lesion of the cord is above the first segment, it is reasonable to expect a traumatic local cord reflex emptying the bladder after a few weeks. In these cases one can temporize with manual expression or intermittent catheterization. Should the fracture be at the sacral segment of the cord, i.e. the first lumbar vertebra, then the parasympathetic innervation is damaged and automatic bladder function cannot develop because the sympathetic is unopposed. In these cases early suprapubic drainage should be instituted and the bladder irrigated from the urethra and out through the suprapubic tube. Prolonged use of a tied-in urethral catheter has drawbacks in that it often sets up urethritis with ascending complications. Intermittent catheterization with all aseptic precautions, including handling the catheter with dissecting forceps only, is safe in these cases even for a prolonged period. 353

Anderson, R. (1932) *Surg. Gynec. Obstet.*, **54**, 207.
Russell, R. H. (1924) *Brit. J. Surg.*, **11**, 491

DISSEMINATED SCLEROSIS

See also Surveys and Abstracts for 1939, p. 316

TREATMENT

Artificial fever. A report by Krusen and Elkins on fever therapy by physical means authorized by the Council on Physical Therapy of the American Medical Association states that, in the few cases of disseminated sclerosis which have received fever therapy, the results have been unfavourable. 354

It must be added, however, that other authorities have reported a favourable influence on the course of the disease.

Krusen, F. H., and Elkins, E. C. (1939) *J. Amer. med. Ass.*, **112**, 1689

DIVERTICULOSIS AND DIVERTICULITIS

See also Surveys and Abstracts 1939, p. 316

STAGES

The Pre-Diverticular State

A complete explanation of the primary cause of diverticulosis has not yet been offered. Rankin and Grimes concluded that neither muscular weakness, neuromuscular dysfunction, increased colonic pressure, vascular stasis, senile degeneration, obesity, nor constipation proved adequate. Spriggs's observations on the pre-diverticular state, confirmed by Hartmann, suggested that there was some preceding process determining the site where multiple diverticula subsequently developed, and pointed out that the deformity of the haustra, which might be considerable, was not easily explained on the view that the lining membrane was in process of 355

passive extrusion at a few weak places by pressure from within. In a piece of colon, of which an extensive area was observed radiologically in the pre-diverticular state, Spriggs found that the circular muscle was less continuous than in the normal colon; the submucosa filled the spaces between the bundles, with at some areas a corresponding protrusion of the mucosa towards the peritoneal surface but at others little or no protrusion. Further, the gaps between the bundles were as evident under a taenia as away from it. This appearance was not seen in the normal colon. I. A. P. Cathie kindly examined microscopically 26 non-diverticulous colons and did not find any break in the musculature such as that shown in Spriggs's slides from cases of early diverticulosis (personal communication). At the next stage, that of formed pouches, Spriggs found that the lining mucosa was as thick in the pouches as in the intestine, the only thinning being at the necks of the pouches where the bundles of the circular muscle fibres were bunched up and thicker. These observations suggested that a local pathological change preceded the formation of the pouches. The pouches were now often discovered by pathologists. According to Bumm one or more diverticula were present at necropsy in every third body over 50 years old.

Diverticulitis

Illustrations continue to be published in which the presence of pouches has been wrongly regarded as evidence of surrounding inflammation, i.e. of diverticulitis, and there is still a lack of appreciation of the ease with which diverticulitis can be recognized by accurate radiology before obstruction, and also of the importance of polypi as a cause of bleeding in a diverticulitic area. Stenholm stated that hardly any other disease of the bowel was so often missed, owing to inconstancy, or lack, of symptoms.

Diverticulitis was not uncommon in women, and Wetherell remarked that it might resemble in all its manifestations pelvic inflammation with in addition the symptoms of low intestinal obstruction. The uterus might be tender, the bladder involved, and the tumour sometimes on the right side, walking or jarring, defaecation, and micturition caused pain. In both sexes the pain radiated downwards (Ledoux Lebard), and the tumour varied in size. Rankin and Grimes laid stress on the importance of bearing in mind the possibility of diverticulitis in cases of perforation, and pointed out that the site of the first pains might be a guide. The incisions made for a supposed appendicitis or ruptured duodenal ulcer were obviously but ill-adapted for a perforation in the left iliac fossa.

Fehr recorded 4 instances of rupture of a diverticulum with an enema, in 2 of the cases with a contrast enema. If the pressure used was not more than a foot, and deep breathing was enjoined, it was not likely to be higher than that normally present in the contracting bowel. In addition to careless douching, Loeper mentioned *purging, riding, and motoring as causes of perforation*.

The X-ray appearances of a chronic perforation into the mesentery, illustrated in Plate IX, Vol. IV, facing p. 216, was described by Ledoux-Lebard as the cauliflower appearance.

Rankin and Grimes estimated that haemorrhage occurred in 16 per cent of the cases of diverticulitis, or more often than in Spriggs's experience. Lockhart-Mummery drew fresh attention to septic complications, such as arthritis, endocarditis, iritis, and *metastatic abscesses in other parts of the body*, a relation to diverticulitis not always being suspected. A direct complication was pylephlebitis simulating Weil's disease, in a man of 34, which was traced at necropsy to a perforation of one of 4 diverticula in the ascending colon (Cooke). Stenholm recorded a case of phlebitis of the inferior mesenteric vein with abscesses in the liver, lung, and muscles.

Further experience confirmed the observation that uncomplicated diverticulitis could often be allayed indefinitely by rest, fluids, paraffin by mouth, and oil enemas. When obstruction threatens a full and careful trial should be given to these measures in all but the most acute and severe cases, before a colostomy is undertaken. In some patients in whom colostomy was advised but refused, Lockhart-Mummery found that appendicostomy, with daily washings, gave relief. In other less severe cases he had freed adhesions and wrapped the affected area in a cuff of omentum, a procedure which he reported as safe, and sometimes useful. As a rule, however, colostomy was the safest and most satisfactory measure for bad cases. Wetherell stated that during acute pelvic inflammations the mortality of colostomy was high, unless the opening was made far away from the inflamed area. In such

cases caecostomy was safest. After colostomy for diverticulitis with sepsis of adjoining tissue, or of the bladder, there should be a long interval—Lockhart-Mummery advised a year—before any local surgical measure was attempted. Abscesses in women should be drained through the rectum if possible, and not the vagina, because of the risk of vaginal fistula.

Resection is only possible for localized disease, not too low in the sigmoid, and when all inflammation has subsided. Lockhart-Mummery resected 17 cases with 4 deaths; the 13 survivors were free of the disease.

Spriggs had from time to time seen a solitary diverticulum of the caecum without any symptom. It was usually larger than multiple diverticula and was harmless unless a concretion caused inflammation. Bennett-Jones described 3 cases of diverticulitis in a solitary caecal pouch, and collected 17 reported cases, 13 were in women, and 11 occurred before the age of 35. Operation was usually undertaken on a diagnosis of appendicitis, or of cancer of the caecum; in some the caecum was resected with that diagnosis. Cases are described also by Hartwell and Cecil, and by Loeper.

Bennett-Jones, M. J. (1937) *Brit. J. Surg.*, **25**, 66.
Bumm, R. (1933) *Arch. klin. Chir.*, **174**, 14
Cooke, W. T. (1937) *Lancet*, **1**, 84.
Fehr, A. (1937) *Zbl. Chir.*, **64**, 676.
Hartmann, J. (1937) *Munch. med. Wschr.*, **84**, 252
Ledoux-Lebard, G. (1937) *Medecine*, **18**, 538
Lockhart-Mummery, J. P. (1938) *Lancet*, **2**, 1401.
Loeper (1937) *Progr. méd., Paris*, **64**, 1442
Rankin, F. W. and Grimes, A. F. (1938) *South. Surgeon*, **7**, 1.
Spriggs, E. I. (1938) *Quart. J. Med.*, **31**, 588.
Stenholm, T. (1938) *Disch. Z. Chir.*, **250**, 19
Wetherell, F. S. (1938) *Amer. J. Obstet. Gynaec.*, **35**, 417.

DROPSY, EPIDEMIC

AETIOLOGY AND PATHOGENY

Hypotheses of Causation

The investigation into the aetiology of epidemic dropsy has been conducted mainly from 3 points of view, namely the hypotheses of deficiency disease, infection, and food-poisoning. 356

Beri-Beri Hypothesis

It is now definitely settled that epidemic dropsy has nothing to do with beri-beri, and no evidence has been adduced in favour of its being a vitamin deficiency disease, cases in which epidemic dropsy and vitamin deficiency co-exist have led to confusion on this point.

Rice Hypothesis

Re-investigation of the part played by rice in the aetiology of epidemic dropsy showed that the 'opacities' in certain samples of rice were not due to an infection; they were found to occur naturally in paddy, and were probably brought into prominence or created by the process of parboiling. The opaque rices were not associated with epidemic dropsy, and there was not any evidence that they were unwholesome. It is, however, possible that an excess of rice in the diet either predisposes to the disease, or aggravates the existing symptoms, e.g. oedema.

Mustard Oil Hypothesis

Lal and Roy produced a syndrome closely resembling epidemic dropsy by feeding volunteers on epidemiologically implicated mustard oil. It was clear that the mustard oil as such could not be responsible for the symptoms, but that either oil expressed from diseased seeds or an adulterant must be implicated. Chopra and his associates re-investigated the whole problem. The study of the fungous diseases of mustard seeds gave negative results. Attention was then concentrated on the study of adulterants in implicated mustard oils. Sarkar's report on the production of symptoms similar to epidemic dropsy by the accidental use as an adulterant of katakar oil (argemone oil) was considered highly suggestive. Kamath described an outbreak of epidemic dropsy in an area where mustard oil was not consumed, in

356 which oil expressed from 'odissmari' seeds was implicated; these seeds were found to be identical with *Argemone mexicana* seeds. The epidemiologically implicated mustard oils almost always gave a positive nitric acid test for argemone oil (Stewart and Boyd, and Lewkowitsch).

In view of these data Chopra and his co-workers fed a batch of 5 volunteers on food cooked in pure mustard oil containing 2 to 10 per cent of argemone oil, and another batch of 4 volunteers on implicated mustard oil; the feeding was continued for 2 to 3 weeks. Symptoms clinically indistinguishable from epidemic dropsy were produced in all the 5 fed on dilute argemone oil and in 2 out of the 4 fed on implicated mustard oil. There was an interval between the stoppage of the oil and the appearance of the oedema varying from 7 to 18 days. Argemone oil was found to be toxic to laboratory animals, but did not produce in them the symptoms of epidemic dropsy. Heating the oil to 240° C. for 15 minutes rendered it non-toxic, though it still gave a strongly positive test for argemone oil.

It is most probable that the substance responsible for the reaction with nitric acid is not associated with the causation of epidemic dropsy. At present it cannot be certainly concluded that epidemic dropsy and argemone oil poisoning are identical. It is also not definitely decided whether or not any other vegetable poison can produce the same symptoms.

Infection Hypothesis

The occurrence of explosive outbreaks of the disease in Bengal and the apparent spread of the disease in a locality after importation of a case led to the idea that an infective agent was responsible for the symptoms, but, even during an epidemic in Bengal, people living on a non-Bengali diet almost always escaped. That an infective agent could spare certain communities and attack almost only Bengalis is beyond comprehension. All attempts to isolate an infective agent from blood and bone marrow have given negative results. The Gram-positive bacilli preponderating in the stools of the majority of early cases were found to be mostly dead, and were also present in at least 10 per cent of patients with disease other than epidemic dropsy. Sera from early convalescent cases of epidemic dropsy did not contain agglutinins in a high titre against the various organisms isolated from the stools. Sections of the skin from mild cases of epidemic dropsy showed definite dilatation of capillaries but no evidence of a virus infection, e.g. inclusion bodies. It is therefore unlikely that the disease is due to a living organism.

Chopra, R. N., Pasricha, C. L., Goyal, R. K., Lal, S., and Sen, A. K. (1939) *Indian med. Gaz.*, **74**, 193.
Kamath, A. V. (1928) *Indian med. Gaz.*, **63**, 555.
Lal, R. B., and Roy, S. C. (1937) *Indian J. med. Res.*, **25**, 239.
Lewkowitsch, J., and Warburton, G. H. (1922) *Chemical Technology and analysis of oils, fats and waxes*, p. 143.
Sarkar, S. L. (1926) *Indian med. Gaz.*, **61**, 62.
Stewart, A. D., and Boyd, J. C., *Public Health Laboratory Practice*, p. 189.

DROWNING; RESUSCITATION

DROWNING

357 Banting *et al.* describe two types of drowning. In type I there is apnoea with an initial struggle, followed by cessation of movement and swallowing, leading to gastric distension. This is followed by vomiting and gasping, when water may be heard to enter the lungs. Somatic activity then ceases. In this type the blood pressure falls suddenly just before death, the heart-rate decreases, fibrillation often occurs, and electrocardiographic activity ceases within 1 or 2 minutes. In type II the initial apnoea continues, and is not followed by gasping, very little water entering the lungs. The blood pressure falls more gradually, the heart-rate decreases 10 to 15 beats per minute, and after a time the ventricular complexes of the electrocardiogram cease; the auricular complexes may, however, persist for 30 to 45 minutes. These experiments indicate the extreme importance of laryngeal spasm. The authors considered the slow heart-rate to be due to vagal influences. Blood-gas analysis showed that the oxygen decreased rapidly to 2 to 3 volumes per cent, and that the carbon dioxide also, after an initial rise, fell, thus confirming the contention of Yandell Henderson.

RESUSCITATION

GENERAL SURVEY

On the basis of their experimental work Banting and his co-workers recommend, in addition to the usual measures, that the larynx should be swabbed with a 10 per cent solution of cocaine hydrochloride, and a catheter passed into the trachea, if there is evidence of laryngeal spasm, as suggested by difficulty in securing a free airway. They also found insufflation of amyl nitrite to be helpful in type II drowning, and emphasize the value of full doses of atropine sulphate ($\frac{1}{60}$ to $\frac{1}{4}$ grain) in combating vagal inhibition, and of adrenaline hydrochloride in large doses (40 minims of a 1 in 1,000 solution). They stress the importance of early and prolonged artificial respiration, urging that it should be continued until rigor mortis sets in. 358

Banting, F. G., Hall, G. E., Janes, J. M., Liebel, B., and Lougheed, D. W. (1938) *Canad. med. Ass. J.*, **39**, 226

DRUG ADDICTION

See also Surveys and Abstracts 1939, p. 318.

AETIOLOGY

A rather rough but suggestive and useful classification of addicts has been given by Neuberger. He divided morphine addicts into (i) morphinomaniacs or true addicts and (ii) morphinists. 359

Psychopathic Origin

Morphinomaniacs are those who resort to the drug in virtue of a kind of predestination due to a defect in their psychical make-up. Clinically they answer to the designation of *petits mélancholiques*: they must have a stimulus from the outside, being incapable of providing it from their own resources. They use the drug to provoke "a momentary suicide". Cure of these subjects is particularly arduous, and they usually relapse.

Secondary or Exciting Causes

On the other hand, in morphinists the habit is not accompanied by a deep-seated need for the poison. Their psychical make-up may not deviate greatly from the normal, and their habit is often due to suffering, i.e. as a sequel to some painful affection, for which the usual analgesics have proved useless. Often the drug has been brought to their notice by their medical attendant or an associate.

TREATMENT

Preventive

The search for a derivative of opium which, while retaining the pain-relieving properties of morphine will not produce euphoria nor induce physical or psychical dependence, as well as the search for some synthetic drug which will serve the same purpose, have for some time been pursued with vigour in the United States. Small and Eddy and their colleagues studied a series of 16 drugs clinically in man, all modifications of the morphine molecule, as well as many synthetic drugs, and much has been learnt of the relationship between chemical structure and pharmacological properties. The analogous endeavour to find a perfect cocaine substitute devoid of addiction properties, although it has resulted in the production of a most useful series of local anaesthetics, has not yet, and perhaps never will, achieve complete success (Small and Eddy *et al.*)

Curative

Detoxication by Direct Withdrawal of the Drug

The method of sudden withdrawal still has its advocates, but no longer is generally accepted as the method of choice; most would reserve it for strong, otherwise healthy young addicts in whom the drug habit is not deeply ingrained nor of long duration. Even so, it is not suitable for application by the general practitioner, and should be reserved for the specialist with command of the facilities of a trained staff in an institution catering for narcophilics. On the other hand, the disadvantages of a too lengthy withdrawal are becoming more widely recognized.

Although the method of gradual withdrawal is practically the only feasible method available for the practitioner who has to treat an addict at his own home, if he can be induced to enter an institution, as is always desirable, there are many drawbacks

359

to too slow a method of procedure. Kolb and Himmelsbach, as the result of their great experience, recommended a rapid withdrawal method which they regarded as the method of choice except for those for whom abrupt withdrawal is suitable. The patients were first stabilized on a few grains of morphine a day (usually not exceeding 4) until they became acclimatized to the new environment. Then the drug was rapidly withdrawn, depending on the circumstances of each case, in from 4 to 14 days, codeine or morphine, or both, in small doses being used to take the edge off the suffering, and prevent collapse. They believe that no healthy person who receives as much as 3 gr. of morphine in small doses between the twenty-fourth and ninety-sixth hour of withdrawal will die whatever may have been the length of habit, degree of physical dependence, or amount taken, provided that he is not given toxic doses of other drugs or subjected to debilitating physical treatment. Fatalities from an excessively severe or unwise procedure undoubtedly occur, though reports of such cases are hard to obtain. Piker and Gelperin stated that in 3 years they had seen 3 deaths from the use of abrupt withdrawal, and Kolb and Himmelsbach collected 12 recorded cases, and suspected that many cases are not reported as they know of 11 such cases, 6 of which occurred in a series of 130 under the hyoscine treatment. As adjuncts, they use warm baths of 10 minutes' duration, 3 times a day: these are of value in decreasing the restlessness, injections of 5 per cent glucose intravenously are also useful for maintaining the water balance and for giving relief from anorexia and irritability. It is important also to treat the insomnia, so often a prominent feature, by paraldehyde, or sometimes by sodium bromide with sodium bicarbonate. Patients given bromides, however, are carefully watched so that the drug can be discontinued on any sign of toxicity.

Special Withdrawal Methods

The results of some valuable researches into the efficacy of various withdrawal methods have recently been published in the United States, where material is abundant. Especially important is a paper by Kolb and Himmelsbach, who attributed the divergent statements made about the worth of any given treatment mainly to the following factors: (i) absence of a proper system of controls, (ii) unsuitable clinical material, and (iii) failure to realize that addicts with the same degree of physical habit reacted to the discomfort of withdrawal with widely different degrees of mental intensity. As regards (ii) it was pointed out that about 80 per cent of the addicts at the present day have such mild habits that they are useless for testing the value of treatments. To obviate the difficulty mentioned under (iii) they have devised 'a simple, impersonal, and quantitative method for estimating the intensity of the abstinence syndrome'. This ingenious method is based upon a system of assessing 'points' both for certain accurately measurable signs, such as rectal temperature, respiratory rate, basal metabolic rate, and blood pressure, and for the presence and intensity of non-accurately measurable signs, such as yawning, lacrimation, perspiration, anaemia, tremor, and restlessness.

Insulin method. The use of insulin in the treatment of the withdrawal symptoms seems to be also receding in favour. Kolb and Himmelsbach, using controls, found that this substance was without any influence on the abstinence syndrome.

The futility of insulin appeared to be shown by the experiments on rats by Stanton, who, while admitting that it is difficult, if not impossible, exactly to duplicate clinical procedures in animals, considered it reasonable to suppose that any real specific treatment should show at least some effect on the course of symptoms produced in animals by withdrawal.

Blister-serum method. Much attention has recently been given to the blister-serum method of Modinos. Kolb and Himmelsbach do not deny that results have been obtained by this procedure, even though the hypothesis upon which it was based is erroneous. Probably the successes obtained were in large measure due to suggestion, and to the fact that the worst period of the withdrawal is tided over by small doses of opium or morphine. The value of suggestion, however, should not be minimized. Vogel, in an interesting research in which he used a modification of the Hull postural method, found that adult male addicts were significantly more suggestible than non-addicts. This increase in suggestibility seems to be due to the narcotic because, after withdrawal, the suggestibility was approximately the same as in normal individuals. A method therefore entailing a good deal of manipulation of the addict might be of value because the addict feels that something definite is being done for him. Moreover, the treatment seems to be harmless if the patient has sound kidneys.

In Great Britain a favourable report upon Modinos's procedure was published by

Margaret Vivian; she uses multiple small blisters (3 or 4 of 1½" square) in preference to one large one and withdraws the fluid before the plaster is removed and reinjects immediately. With these precautions no pain or reaction of any kind followed. 359

Lecithin method.—Chopra and Chopra, and Chopra and Ganguly reported considerable success from the use of a modification of the lecithin treatment of the abstinence syndrome originally introduced by Ma, especially when combined with intravenous injections of glucose. Using an abrupt withdrawal method, they gave ovolecithin in pill form, 10 grains 3 times a day for 5 consecutive days. Except in the slighter cases, an intravenous injection of glucose was also given every morning (repeated if necessary in the evening) for the first 3 or 4 days. The amount of each injection was 25 c.cm. of 25 per cent glucose. The injections were then stopped but glucose, if required, was continued by mouth. A diet rich in proteins and lecithin was also prescribed.

In a series of 200 cases there was 'complete cure' in 140, or 70 per cent, and complete failure in only 10 per cent, the remainder being benefited. The cure, in cases of ordinary severity, took about 10 days, but in more severe cases, or in older persons, it might be prolonged to 2 or 3 weeks. Relapses did not appear to have been frequent.

Whether or not a comparable success would be obtained with cases of addiction as met with in Great Britain is difficult to decide, and no reports appear to be available. It must first be noted that the authors did not report any control series; only 2 of their patients were morphine addicts, the rest being opium eaters with 2 smokers; moreover, a very careful judicious symptomatic treatment was used as an auxiliary. Further, as Kolb and Himmelsbach point out, the theoretical basis of the treatment seems to rest upon none too sure a foundation, though Chopra and Ganguly maintain from their observations that lecithin tones up the nerves of the addicts, and glucose helps to restore disturbed water-balance. The treatment, however, is simple and might perhaps be given a trial here as an auxiliary, especially if the Chopras' contention is correct that it can be carried out in the addict's house if his faithful co-operation is assured. The wisdom of abrupt withdrawal of the narcotic drug in these circumstances is, however, open to question.

Rossium method.—The drug rossium also finds scant favour with them.

Drugs of the atropine series.—It was found that treatment by the belladonna group of drugs, i.e. belladonna, atropine, and hyoscine, not only was useless but aggravated the sufferings of the patients, and some of the withdrawal fatalities were attributable to the use of these drugs.

The so-called 'eliminative' treatments, e.g. excessive purgation and the use of pilocarpine, were also condemned. It is pointed out that, if these measures are successful in the elimination of morphine, this constitutes a very good reason for avoiding their use, because during withdrawal the organism suffers from abstinence, rather than from the presence of morphine in the body.

Strychnine is also contra-indicated because these patients are hypersensitive, and strychnine aggravates this.

Chopra, R. N., and Chopra, G. S. (1937) *Indian med. Gaz.*, **72**, 265.
— and Ganguly, S. C. (1939) *Indian J. med. Res.*, **28**, 699.
Kolb, L., and Himmelsbach, C. K. (1938) *Publ. Hlth Rep. Wash.* Suppl. No. 128.
Neuberger, L. (1938) *Mouvem. sanit.*, 393.
Piker, P., and Gelperin, J. (1937) *Ann. intern. Med.*, **10**, 1279. (Abstr. in *J. Amer. med. Ass.* (1937), **108**, 1746.)
Small, L. F., Eddy, N. B., Mosettig, E. and Himmelsbach, C. K. (1938) *Publ. Hlth Rep. Wash.*, Suppl. No. 138.
Stanton, E. J. (1937) *J. Pharmacol.*, **60**, 387.
Vivian, M. (1937) *Lancet*, **1**, 1221.
Vogel, V. H. (1937) *Publ. Hlth Rep. Wash.* Suppl. No. 132.

DRUG ERUPTIONS

See also Surveys and Abstracts 1939, pp. 176 and 319.

COMMON DRUG ERUPTIONS

Iodides

That bullous iodide eruptions are particularly liable to occur in subjects of cardiac and renal disease has long been known. Adamson reported 3 more cases of iodide 360

360 eruptions in patients with bacterial endocarditis and renal disease from St. Bartholomew's hospital; all of these were fatal. In one patient, the eruption appeared after the administration of a total of 90 grains of potassium iodide. The second was a man aged 34, in whom blisters developed after 7 doses each of 5 grains of potassium iodide. In the third patient, aged 40, the eruption appeared after one dose of 5 grains of potassium iodide, and showed that defective elimination cannot be the main factor in causation, as only 5 grains of potassium iodide had been ingested.

Sulphanilamide

Sulphanilamide has been responsible for various eruptions, erythematous or urticarial, in macules, papules, or larger lesions and even exfoliative dermatitis. Since the drug can induce sensitization of the skin to light, some eruptions are due to a combination of both factors

Adamson, H. G. (1938) *Brit. J. Derm.*, **50**, 167.

DWARFISM AND INFANTILISM

362 See Surveys and Abstracts 1939, p. 319

DYSENTERY, BACILLARY

See also Surveys and Abstracts 1939, p. 320

BACTERIOLOGY OF THE DYSENTERY GROUP OF BACILLI

The Mannitol-Fermenting Group

364 Recent work has clarified ideas regarding the nature and classification of the mannitol-fermenting group of dysentery bacilli

The *B. dysenteriae* Sonne subgroup which produces acid in lactose and saccharose after some days of incubation remains unchanged. *B. dysenteriae* Sonne is the only member known to be pathogenic; other organisms giving these biochemical reactions, but of different antigenic structure, are not uncommonly isolated from normal stools.

The *B. dysenteriae* Flexner subgroup has now been clearly defined. It has been shown that the organisms previously included in this subgroup possess a common group antigen, and that each valid type has an individual type antigen. Accepting the possession of this group antigen as the essential characteristic of the Flexner subgroup, 2 further types, identified in India, and now found in various parts of the world, have been included. Further, the so-called Newcastle bacillus is for the same reason included, despite its anomalous biochemical reactions. This is justified by the fact that its antigen (type specific plus Flexner-group) is common to several strains, one being identical with classical Flexner, another being the commonest member of the so-called *alkalescens* subgroup, and a third being the Manchester bacillus which produces acid and gas in glucose, mannitol, and dulcite; it is considered that the strain giving true Flexner biochemical reactions is the original type, and that the others are "biochemical" variants. It is proposed, when investigations are complete, to allot numbers to the various types in this Flexner subgroup. A number of unclassified types remain which have the biochemical reactions of the Flexner subgroup but which do not possess its group antigen. These, together with certain late fermenters of dulcite, previously included in the *alkalescens* subgroup, may be placed for the present in a loose subgroup. There is conclusive evidence that certain of these types cause bacillary dysentery. So far (with one unpublished exception) they have not been reported outside India.

Boyd, J. S. K. (1936) *J. R. Army med. Cps.*, **66**, 1
(1938) *J. Hyg., Camb.*, **38**, 477

DYSIDROSIS

366 See Surveys and Abstracts 1939, p. 320

DYSMENORRHOEA

367 See Surveys and Abstracts 1939, p. 321.

DYSPEPSIA

See Surveys and Abstracts 1939, p. 321. 369

DYSPNOEA

See Surveys and Abstracts 1939, p. 322. 373

EAR DISEASES

See also Surveys and Abstracts 1939, pp. 86 and 322. 374-384

OTOGENOUS INFECTIONS

Treatment

Sulphonamide Drugs

The application of drugs of the sulphonamide group has marked a very great advance in the treatment of certain types of otitic infection. J. I. Maybaum *et al*, while agreeing as to the great value of these drugs, urge that their indiscriminate use may mask the clinical picture, and that they often effect a latent course of the disease. Because of their tendency to obscure the course of the infection, they should be used cautiously, if at all, in acute otitis media. The authors state that the use of sulphonamide drugs is inadvisable during the course of a suspected mastoiditis before operation and also post-operatively, unless in the presence of a complication such as meningitis, sinus thrombosis, and brain abscess.

They give the following indications for the use of sulphonamide drugs in ear infections: in the presence of impending otitic meningitis from whatever cause, a sulphonamide drug should be given at once; in the case of otitis media, before suppuration has occurred, it may be given cautiously.

Maybaum, J. I., Snyder, F. R., and Coleman, F. F. (1939) *J. Amer. med. Ass.* **112**, 2589.

ECZEMA

See also Surveys and Abstracts 1939, pp. 63 and 326. 386

CLINICAL PICTURE

True Primary Eczema

'White Line'. Whitfield recently reviewed the subject of the white reaction (white line) in skin diseases, and concluded that this reaction was caused by contraction of the superficial capillaries in response to the release of a constrictor substance in the superficial part of the skin along the line of contact of the stroking stimulus.

Whitfield, A. (1938) *Brit. J. Derm.*, **50**, 71.

ELECTROTHERAPY

See also Surveys and Abstracts 1939, p. 326. 389

LOW-VOLTAGE VARYING CURRENTS

Faradic Currents

Constipation and Obesity

The heavy, expensive, and considerably cumbersome Bergonié apparatus for faradic stimulation of many groups of muscles simultaneously has recently been modified so that treatment practically identical with the complicated Bergonié treatment can now be given by any medical practitioner, masseuse, or even by the patient after suitable instruction. This chair is manufactured in London. Its advantages are compactness, incorporation of modern principles of making the current, and greatly improved electrodes, with consequent economy in prime cost, care, and management. A great reduction in the expense of care and maintenance is also secured.

389

HIGH-FREQUENCY CURRENTS

Short-Wave Current

Short-wave therapy was formerly regarded as the best for chronic infections of the accessory nasal sinuses, there have, however, been some accidents with resulting permanent damage to the ears and to the pituitary by the passage of short waves through the sinuses, thereby overheating the structures at the base of the brain. To avoid this, the disc electrode supplied with most modern short-wave apparatus can be used, the indifferent electrode, a pad, being placed on the floor, or even in front of the patient, so that the short waves pass through the antrum or sinuses close to the disc electrode, and not through the whole thickness of the head. Intensive short-wave therapy given for middle-ear deafness, through from ear to ear, has resulted in a patient, formerly partly deaf, becoming completely deaf in both ears.

EMPHYSEMA OF THE LUNGS

390-395 See Surveys and Abstracts 1939, p. 327.

ENCEPHALITIS EPIDEMICA

See also Surveys and Abstracts 1939, p. 327

PATHOLOGY

399 The disease, encephalitis Type A, has been suspected to be due to a virus which gained access to the central nervous system from the nasopharynx. The infective agent has not been demonstrated but is probably distinct from those causing epidemic encephalitis Type B of the Japanese (1912–29) and St. Louis (1933) epidemics, and Australian 'X' disease (1917–18). The age incidence in the former 2 is chiefly in adult life and in the latter in early childhood, but in none of these conditions are ocular palsies common, nor the Parkinsonian state, and residual defects are rare.

ENCEPHALO-MYELITIS

See also Surveys and Abstracts 1939, p. 328

ACUTE DISSEMINATED ENCEPHALO-MYELITIS COMPLICATING THE SPECIFIC FEVERS AND VACCINATION

Nervous Complications of Vaccination, Measles, Smallpox, Chicken-pox, and German Measles

400 Up to 1936, about 120 cases of nervous complications following varicella have been reported (Underwood). About 18 cases following German measles have been reported (Read), with ages from 3 to 33 years, demyelination was recorded post-mortem in one case, and perivascular lymphocytic cuffing and oedema in another.

Mumps Meningo-Encephalo-Myelitis

Dopter's view that the virus of mumps is primarily neurotropic was supported by the fact that the cerebrospinal fluid of contacts about the fifteenth day might show a lymphocytic increase whether parotitis developed later or not (de Lavergne, Kissel, and Accover). Finkelstein found that the cerebrospinal fluid of cases of mumps with no symptoms referable to the nervous system showed an increase of protein and had lymphocytic cell counts of 10 to 880.

SPONTANEOUS ENCEPHALO-MYELITIS

In addition to the virus infections, such as poliomyelitis, epidemic encephalitis Type A, rabies, and herpes zoster, many others have recently been recognized—epidemic encephalitis Type B of Japan, St. Louis encephalitis of 1933, and Australian 'X' disease. Others, unlike poliomyelitis the virus of which primarily affects man, appeared to be infections of animals but capable of transmission to man, for example swineherds' disease, a benign lymphocytic meningitis, 'louping-ill' of sheep—possibly related to Australian 'X' disease, 'equine encephalitis' of North

America (Webster and Wright), and the virus of acute chorio-meningitis or benign lymphocytic meningitis found in mice.

Equine encephalitis

Equine encephalitis, epidemic in certain parts of North America, could be transmitted to man. Two serologically and epidemiologically different strains were recognized, the eastern and western types. During epidemics cases of encephalitis occurred among infants and children (Webster and Wright). Fothergill, Dingle, Farber, and Connerley recovered the eastern strain of equine encephalitis virus from the brain of a child, aged 7, who died of encephalitis; her cerebrospinal fluid showed 2,000 cells, with 85 per cent polymorphonuclears, and 0·19 g. protein. The emulsified brain tissue was injected into mice, death following in 48 to 72 hours. Using a 1 in 1,000 dilution of the mouse-brain emulsion and injecting intracerebrally, 2 guinea-pigs actively immunized against the eastern strain remained well; 1 guinea-pig actively immunized against the western strain died, and 3 controls all died. The histological evidence verified the diagnosis of encephalitis.

Wesselhoeft, Smith, and Branch reported that, after an outbreak of equine encephalitis causing the death of 200 horses in south-east Massachusetts and Rhode Island, 24 human patients were recorded. Of these 8 were admitted to hospital and all died. Their ages varied between 50 years and 10 months. The symptoms were those of any acute encephalitis, but hyperpyrexia was invariable and the course of the disease was short—3 to 4 days. The cerebrospinal fluid showed a high cell-count, but no constancy in the predominating type of cell, and a moderate rise of protein. The virus was recovered in several cases. Histological findings were constant, namely, intense engorgement of all cerebral and meningeal vessels; blood vessels showed intense perivascular cuffing, with polymorphonuclears frequently predominating in the infiltrations; there was diffuse infiltration of the cortex, basal ganglia, pons, medulla, and cervical portions of the cord, and also discrete and confluent areas of necrosis.

Eklund and Blumstein reported 6 cases of encephalitis in patients who had been in contact with sick horses. The symptoms were abrupt onset of headache, vomiting, dizziness, drowsiness, and fever. Two patients died in 4 to 5 days. Blood from 3 patients who recovered was tested against the western strain of equine encephalitis and the serum of one neutralized it.

Acute Benign Lymphocytic Meningitis

The virus associated with this condition by Armstrong and Dickens has been proved to be identical with the European type by Findlay, Alcock, and Stern. Monkeys and mice experimentally inoculated with the virus could be protected by the blood serum of human convalescents. Healthy mice are probably the carriers of infection. The name lymphocytic chorio-meningitis was used to describe the condition in experimental animals. The virus of benign lymphocytic meningitis was first isolated (Armstrong and Lillie) from a fatal case in the St. Louis epidemic of encephalitis (1933), was found to be pathogenic for monkeys and mice, but was not supposed to be the virus responsible for the actual epidemic of encephalitis in St. Louis.

Armstrong, C., and Dickens, P. F. (1935) *Publ. Hlth Rep. Wash.*, **50**, 831.
Eklund, C. M., and Blumstein, A. (1938) *J. Amer. med. Ass.*, **111**, 1734.
Findlay, G. M., Alcock, N. S., and Stern, R. O. (1936) *Lancet*, **1**, 650.
Finkelstein, H. (1938) *J. Amer. med. Ass.*, **111**, 17.
Fothergill, L. D., Dingle, J. H., Farber, S., and Connerley, M. L. (1938) *New Engl. J. Med.*, **219**, 411.
de Lavergne, V., Kissel, P., and Accoyer, H. (1938) *Bull. Acad. Méd. Paris*, **119**, 534.
Read, C. F. (1937) *J. Amer. med. Ass.*, **109**, 654.
Underwood, E. A. (1935) *Brit. J. Child. Dis.*, **32**, 83.
Webster, L. T., and Wright, F. H. (1938) *Science*, **88**, 305.
Wesselhoeft, C., Smith, E. C., and Branch, C. F. (1938) *J. Amer. med. Ass.*, **111**, 1735.

ENDOMETRIOSIS AND ADENOMYOMA

See also Surveys and Abstracts 1939, p 329.

MORBID ANATOMY AND PATHOGENESIS

Definition

401 There has been a tendency in the last year or two to speak of uterine endometriosis as internal endometriosis, and extra-uterine endometriosis as external endometriosis.

Extra-Uterine Endometriosis

Frankel and Schenck propound the view that, when an ectopic pregnancy develops in the tube or elsewhere, pre-existent ectopic endometrial tissue is always present at that site. The fertilized ovum, drawn by positive chemiotaxis, becomes embedded in a patch of endometrium which in this event is ectopic. Ectopic pregnancies are always primary and never secondary; i.e. when ovarian, abdominal, or intra-ligamentary pregnancies occur this is due to the fertilized ovum becoming embedded in ectopic endometrium at those sites, and not to re-implantation of an ovum which was originally tubal but has become detached. Endometrial tissue could be demonstrated in specimens removed from an ectopic pregnancy, unless there had been excessive destruction of tissue from haemorrhage.

Navratil and Kramer described a case of endometriosis, suspected to be such on clinical grounds, and confirmed histologically, in the extensor carpi radialis of the right elbow. This was difficult to explain on the usual hypotheses, and might have been due to metastatic or embolic endometriosis through the lymphatics or veins.

CLINICAL ASPECTS

Association with Sterility

From analysis, particularly from the point of view of sterility, of 159 cases operated on at Helsingfors, Turunen concluded that, although in some cases sterility associated with endometriosis is due to genital hypoplasia, it is also sometimes due to the endometriosis i.e. to the proliferation of connective tissue which it causes. A conservative operation was possible in 66 cases out of 159, and of these 21 subsequently became pregnant, this is considered a very good result, as the average period of sterility was lengthy. The condition should be diagnosed at the earliest possible moment while conservative operation is still feasible.

Frankel, J. M., and Schenck, S. B. (1937) *Amer. J. Obstet. Gynaec.*, **33**, 393.
Navratil, E., and Kramer, A. (1936) *Klin. Wschr.*, **15**, 1765.
Turunen, A. (1938) *Acta obstet. gynec. scand.*, **18**, 237.

ENDOMETRITIS, CERVICITIS, AND METRITIS

402-405 See Surveys and Abstracts 1939, p 330.

ENDOSCOPY OF THE RECTUM

SIGMOIDOSCOPY

Instruments

406 An improved sigmoidoscope of the Morgan and Officer type is now available. It is made with tubes of 3 diameters, the two smaller ones are $\frac{5}{8}$ in. and $\frac{1}{2}$ in. respectively, so that they can be passed through a narrow anal canal or a stricture of the rectum. A magnifying attachment can be applied to the outer end of the instrument, and gives an excellent view, even with these very small sizes.

Vol. V ENDOSCOPY OF THE UPPER RESPIRATORY AND URINARY TRACT

412, 413 See Surveys and Abstracts 1939, p 330.

ENTERIC FEVERS

417-419 See Surveys and Abstracts 1939, p 330.

EPILEPSY

See also Surveys and Abstracts 1939, pp. 124, 126, and 331.

TREATMENT

432 Sodium diphenylhydantoinate (epanutin) has been found to be of use in controlling seizures in some patients who do not respond to other forms of treatment and in those whose attacks are frequent. This treatment is still in the experimental stage, but favourable reports have been published from America. Merritt and Putnam introduced the drug, as a result of experimental trials on animals of the anti-convulsive action of many substances, and they report that in 142 cases of major epilepsy attacks ceased in 58 per cent. and in cases of *petit mal* in 35 per cent.

This drug is closely related to nirvanol. It produces toxic effects (e.g. ataxy, tremors, diplopia, dermatitis, and purpura) but these disappear on cessation of treatment.

The optimal dosage varies. In patients above the age of 6 the initial dose should be 0·1 gram 3 times daily, with or immediately after meals. The maximal dose is 0·6 gram daily. Infants and children up to the age of 5 should receive an initial dose of 0·1 to 0·2 gram daily; this may be gradually increased to 0·3 or 0·4 gram daily.

Blair, Bailey, and McGregor tested epanutin on 53 male and 22 female chronic epileptics and confirmed the conclusions of Merritt and Putnam that the drug is a strong anticonvulsant. They reported, however, more toxic reactions, including nausea, delusions, hallucinations, confusion, clonic spasms, agitation, and mental depression. When a patient has been under treatment with other drugs the method of change-over which they recommend is to substitute one dose of the previous drug by one capsule of epanutin every second day, the patient is then receiving epanutin alone on the sixth day if he has been receiving 3 doses daily, or on the eighth day if 4 doses daily. They found marked variation between patients in their response to the drug, both as regards control of fits and idiosyncrasy to its toxic action.

Steel and Smith also report 20 chronic cases treated with epanutin and find a similar variation in response. They consider that in some cases the drug is superior to others, and recommend further trials. They found that the drug delayed the seizures, but did not greatly alter the number of the fits, and that a patient treated with epanutin might have no fits for 8 or 10 days, and then have several in close succession.

Blair, D., Bailey, K. C., and McGregor, J. S. (1939) *Lancet*, 2, 363.
Merritt, H. H., and Putnam, T. J. (1938) *J. Amer. med. Ass.*, **111**, 1068.
Steel, J. P., and Smith, F. S. (1939) *Lancet*, 2, 366.

EPIPHYSES, DISEASES AND INJURIES

See Surveys and Abstracts 1939, p. 334 **434-438**

EPISTAXIS

See also Surveys and Abstracts 1939, p. 334.

TREATMENT

439 In connexion with the treatment of difficult cases of epistaxis Davis described in detail the blood supply of the nose and pointed out that the upper part is supplied by the internal carotid and the lower part by the external carotid. The volume of blood circulating in the nose was affected by changes in temperature and in the position of the head, physical and mental exertion, and emotion. Patients with severe epistaxis should therefore be kept at rest in a sitting position, and change of temperature avoided. For spontaneous epistaxis in old people Davis recommended first sitting the patient upright with the head depressed and the nostrils compressed by finger and thumb. A pledget of wool soaked in 20 per cent cocaine hydrochloride should then be placed on the septum, and after its removal the nostril packed with the narrowest ribbon gauze soaked in 20 per cent cocaine hydrochloride solution with an equal quantity of adrephine inhalant. After 10 minutes the gauze should be removed; then if the bleeding point is visible, it can be sealed by the dull

439 red galvano-cautery or by gauze impregnated with ferropyrine powder. The gauze plug should not remain longer than 24 hours without removal or replacement. If local treatment fails, morphine sulphate ¼ grain should be given. For epistaxis associated with disorders of the blood, such as anaemia and leukaemia, Davis recommended blood transfusions, intravenous haemostatic serum, and morphine. The inflated rubber bag was the best method of control in multiple telangiectasis.

Davis, E. D. D (1939) *Brit. med. J.*, **1**, 721.

ERUPTIONS, ANOMALOUS AND ATYPICAL

See also Surveys and Abstracts 1939, p. 334.

ANOMALIES OF THE HAIR AND NAILS

440 Thinning of the nails, koilonychia, appears to be due to deficiency in the amount of serum iron. It has been stated that in pernicious anaemia the serum iron is not low, although the total haemoglobin is diminished. Barber (unpublished communication) has seen a case of thinned nails associated with a low serum iron, but not with anaemia, the condition disappeared after administration of iron.

ERYSIPELAS

441 See Surveys and Abstracts 1939, p. 335.

ERYTHEMA

See also Surveys and Abstracts 1939, p. 335.

CLINICAL PICTURE

Erythema due to Internal Causes

Erythrodermia

442 Neumark reported generalized exfoliative erythrodermia in a woman, aged 36, after ingestion of 15 capsules of male fern for tapeworm infestation.

Gattwinkel described the association in a woman, aged 72, of primary generalized leukaemic erythrodermia with the blood picture of lymphoid leukaemia, but without any clinically discoverable changes in the liver, spleen, or other internal organs. He discussed the relation between lymphoid leukaemia and erythrodermia and stated that, among the records of 222 cases of lymphoid leukaemia of the skin, in 4·5 per cent the skin condition was primary, and that in half of this 4·5 per cent there was no subsequent involvement of the internal organs. The erythrodermia in these cases was regarded as an early manifestation of leukaemia.

Gattwinkel (1937) *Arch. Derm. Syph., Wien*, **175**, 578.
Neumark, S. (1938) *Derm. Wschr.*, **106**, 331.

ERYTHRAEMIA

443 See Surveys and Abstracts 1939, p. 336.

ERYTHROMELALGIA

445 See Surveys and Abstracts 1939, p. 337.

EYE EXAMINATION

456, 457 See Surveys and Abstracts 1939, p. 337.

EYE, HEREDITARY DISEASES

INHERITED EYE DEFECTS

Nystagmus

458-472 A survey of hereditary eye diseases in Tasmania has been made by Hamilton. One pedigree in his essay pointed out the relation of stuttering to nystagmus. He

also reported a family in which the father and two sons had congenital nystagmus; one of the sons had poor central vision with marked nystagmus on looking ahead, diminishing when he looked to the side; the other son had good central vision, the nystagmus being exaggerated when he looked to the side. 472

Other conditions

Posthumus has drawn attention to the familial association of megalocornea with other anomalies and recorded a family with several examples of megalocornea chiefly affecting men, diabetes mellitus chiefly affecting women, and deafness in both sexes. In some cases atrophy of the vitreous and pigment disturbance of the iris were associated with megalocornea. Defective hair pigment was also noted.

Hamilton, J. B. (1938) *Brit. J. Ophthal.*, **22**, 19, 83, and 129.
Posthumus, R. G. (1939) *Klin. Mbl. Augenheilk.*, **102**, 1.

EYELIDS, INJURIES AND DISEASES

See Surveys and Abstracts 1939, p. 338. 473-482

FALLOPIAN TUBES DISEASES

See Surveys and Abstracts 1939, p. 338. 483-486

FIBROSITIS

CLINICAL PICTURE

Bursitis

Olecranon bursitis is due to gout in a large proportion of cases. 489

Brachialgia

Vol. V, p. 286, 1st paragraph of this section, 2nd sentence should read: The structures most commonly affected are the subacromial bursa, the supraspinatus tendon, the sheath of the biceps tendon . . .

Pectoral Fibrositis

Dixon emphasizes the importance of avoiding the erroneous diagnosis of angina of effort in cases of pectoral fibrositis. Symptoms of fibrositis may respond to nitroglycerin and so appear to confirm the mistake. If anginal symptoms are present in the absence of cardiovascular symptoms, fibrositis should be looked for; cardiac abnormalities, however, may be associated. The fibrositis should be treated by breaking up the nodules with the fingers at least 4 times a week for 2 weeks.

Dixon, R. H. (1938) *Brit. med. J.*, **2**, 891.

FILARIASIS

See also Surveys and Abstracts 1939, p. 340.

FILARIINAE

Wuchereria bancrofti

Treatment of Lymphangitis

Recent reports on treatment of lymphangitis by sulphonamide compounds, notably prontosil, in full doses are distinctly favourable and merit further trial. 491

Filaria malayi

The life history of the mosquitoes (*Mansonioides*) concerned in the transmission this organism is an excellent example of scientific oecology, because the larva is provided with a special respiratory syphon to enable it to absorb oxygen from the roots of *Pistia stratiotes*, a water plant on which it lives. The prevention of this disease is therefore intimately connected with the eradication of this plant.

The paragraph on distribution (foot of p. 313, Vol. V) should be replaced by the following: The distribution of this filaria, as at present known, is Java, Sumatra and other islands of the Malay Archipelago, south India, Ceylon, and southern China.

Iyengar, M. O. T. (1937) *Indian med. Gaz.*, **72**, 300.

FLUKE INFECTIONS, INTESTINAL

FASCIOLOPSIASIS

Life Cycle

497 According to Kuang Wu the cercariae of *Fasciolopsis buski* may become encysted on almost any plant that grows in stagnant water and as many as 20 encysted metacercariae may be found on a single leaf, on *Salvinia natans* and *Spirodela (Lemna) polyrhiza*, plants which float on the surface.

Treatment

McCoy and Chu treated 129 children whose faeces showed eggs of *F. buski* with hexylresorcinol. The dosage was 0·4 gram for children under 7, to 1 gram for those over 13. Re-examination of the patients 2 to 3 weeks later showed that eggs were absent in 54 per cent, and that in all but 5 per cent their numbers had been reduced by at least one half.

HETEROPHYES HETEROPHYES

Pathology

500 Infection with these flukes causes a few minor symptoms; intermittent diarrhoea has been described.

Kuang Wu (1937) *Ann. Parasit. hum. comp.*, **15**, 458.
McCoy, O. R., and Chu, T. C. (1937) *Chin. med. J.*, **51**, 937.

FOETUS DISEASES, MALFORMATIONS AND MONSTROSITIES

See also Surveys and Abstracts 1939, p. 340

ABNORMAL CONDITIONS OCCURRING IN LIVING FOETUS

Skeleton

Amelia

508 That absence of limbs, complete or partial, is a Mendelian recessive character was evidenced by the case of a Brazilian family, in which 6 out of 12 children of two normal parents (who were, however, closely related—either uncle and niece or, according to local gossip, brother and sister) were born without hands and feet.

Genito-Urinary System

Pseudo-hermaphroditism as a Mendelian character

Several cases have been recorded of pseudo-hermaphroditism, masculine as well as feminine, in each member of a pair of twins (Schwalbe), and Feldman saw a case (unpublished) in which the anomaly occurred in two sibs who were not twins.

Situs Inversus

As a Mendelian Recessive

Additional evidence that situs inversus is a recessive character was afforded by the case recorded by Pezzi and Carugati, in which the condition was present in 2 twin brothers. On the other hand, Dubreuil-Chambardel found the condition in one member only of a pair of monozygotic twins, and Ostertag and Spaich recorded a case of congenital dextrocardia alone in one member only of such a pair of twins. It appeared therefore that in monozygotic twins the condition might occur as a stereoisomerism and not as a genetic character.

DOUBLE MONSTERS

Classification

Nomenclature of Double Autosites

510 *Heterosexual conjoined twins.*—Another case of thoracopagous twins in which one foetus (right) had the external genitalia of a female and the other (left) those of a male, with normal penis 2 cm. long, and urethra, as well as rudimentary scrotum—

in which, however, no testes could be felt—was delivered by Blasius Szendi of Debrecen, Hungary, in February 1938; this case will be published in full but he kindly stated that the gonads of each foetus were ovaries, and that each also had a uterus and tubes; there was no prostate in the apparent male. In addition, the adrenal cortex of each foetus contained the fuchsinophil cells found in pseudo-hermaphrodites (see Vol. V, p. 367). The right foetus, therefore, was a normal female, and the left was a feminine pseudo-hermaphrodite. But, since pseudo-hermaphroditism is a Mendelian character (see Vol. V, p. 367 and above), the difficulty of explaining the monozygotic origin of this thoracopagus still remains.

Physiology

Double Autosites

Dermatoglyphics. Dr. A. D. Hodges of Sokoto, Nigeria, in September 1937, obtained the fingerprints of the 19 months' old sternopagous sisters who had been successfully separated by Dr McLaren in June 1936. Analysis of these prints did not show any striking similarity between the patterns of the corresponding fingers of either homolateral or heterolateral hands, such as was seen in monozygotic twins (unpublished).

Blood-groups Whether conjoined twins are uni- or bi-ovular, the 2 members of a pair should always belong to the same blood group, so long as there is any considerable circulatory intercommunication between them. In twins, however, in which the circulatory interchange is very slight, it is conceivable that the 2 members of a pair should belong to different groups, if they are of binovular origin. Drs. A. D. Hodges and James Hilton Brockway, of the Medical Department of Sokoto, Nigeria have, at Feldman's request, carried out independently in September 1937 and in February 1938 respectively, the blood grouping of the sternopagous twins that had been successfully separated by Dr. McLaren in June 1936. Their results agree in showing that each of the twins at the ages of 19 months and 24 months belonged to group B. This was, as far as is known, the first time that such an investigation had been made on conjoined twins, but the result did not necessarily prove the monozygotic origin of the pair. If a similar case, with very slight circulatory interchange, could be found in which the 2 components belonged to different blood groups, the proof of their binovular origin would be well-nigh complete.

Situs Inversus in One Member Only of a Pair of Conjoined Twins

There seems to be no doubt that situs inversus in the right member alone of a pair of conjoined twins is not uncommon, especially in thoracopagi. This phenomenon is somewhat difficult to explain. Ordinarily situs inversus occurs as a Mendelian recessive (see above) and therefore its occurrence in one member only of such a pair should be conclusive evidence of their binovular origin. On the other hand, the facts that when such situs inversus was present in conjoined twins it always occurred in the right member only, and that it was sometimes found in one member only of a pair of ordinary separate identical twins (Dubreuil-Chambardel, and others), led to the conclusion that in such cases it was a stereoisomerism, i.e. a mirror-image phenomenon. But, if this were the case, such stereoisomerism would be expected in all conjoined twins, as well as in all identical twins; this is not the case.

Dubreuil-Chambardel, L. (1927) *Pr. méd.*, **35**, 1157.
Kochler, O. (1936) *Z. KonstLehre*, **19**, 670.
Ostertag, M., and Spaeh, D. (1936) *Z. KonstLehre*, **19**, 577.
Pezzi, C., and Carugati, L. (1924) *Cuore e Circul.*, **8**, 361.
Schwalbe, E. (1906) *Die Morphologie der Missbildungen des Menschen und der Tiere*, 1ter Teil, *Allgemeine Missbildungslehre (Teratologie)*, Jena

FOOD

See Surveys and Abstracts 1939, p. 341. 513-518

FOOT, DISEASES AND DEFORMITIES

See Surveys and Abstracts 1939, p. 342. 520-527

FUNGOUS DISEASES

See also Surveys and Abstracts 1939, p. 342.

RINGWORM INFECTIONS

AETIOLOGY

529-535 A culture of *Trichophyton gypseum*, the dermatophyte causing 67 per cent of the ringworm in Alberta, was obtained by Dowding and Orr from scales taken from the fingers of a patient with ringworm of the hand. After verification by other medical mycologists the strain was used as a type-culture in the reported investigation.

Fifteen other cultures isolated from infected tissue of patients with 3 different types of ringworm were identified as *T. gypseum*. The criteria for identification were the gross appearance of the cultures, the microscopical character of the mycelium and spores; and the occurrence of hyphal fusions between the fungus in question and the type-culture.

The 3 clinical types of ringworm demonstrated as due to *T. gypseum* were vesicular lesions of the glabrous skin (7 patients with lesions on the hand, wrist, and shoulder); chronic, scaly, sometimes vesicular lesions of the skin of the feet (5 patients); and pustular, boggy, nodular lesions of the beard with hair infection (3 patients), or kerion of the scalp (one patient).

Nine of the 16 cultures of *T. gypseum* differed from the type-culture in texture or colour of the mycelium, in pigmentation of the nutrient medium, or in microscopical characters such as the absence of macroconidia. No correlation existed between the clinical type of ringworm caused by the fungus, and the variation which it exhibited on Sabouraud's medium.

Strains of *T. gypseum* isolated from different patients vary one from another, and any individual strain varies with age. Emmons, working with cultures of *Achorion gypseum* derived from a single uninucleate spore, obtained 6 variants which differed so markedly in colour and texture from the parent culture that, had they been derived from different patients, they would almost certainly have been described as different species. He obtained the same type of variants from the stock cultures of *T. gypseum*.

Sabouraud created a number of species of dermatophytes which he placed under the '*gypseum*' group of Trichophyta. They are distinguished from one another only by differences in colour and texture of the cultures. In the light of recent research some of them and also *T. interdigitale* may well be variants of a single species.

Whereas in Alberta the commonest dermatophyte was *T. gypseum*, which formed 67 per cent of the cases, in Winnipeg, 800 miles east, *T. gypseum* was responsible for only 7 to 8 per cent of the fungous diseases, and in Vancouver, 800 miles west, Cleveland found no *T. gypseum* whatsoever.

RINGWORM OF SCALP

Treatment

The epilating and toxic actions of seven salts of thallium were studied by Torres experimentally and then clinically on 129 cases of ringworm in children. Thallium acetate had the additional disadvantage of being hygroscopic. The cyclic compounds (benzoate, salicylate, and acetylsalicylate) were the least toxic in the series. Epilation closely depended on the amount of metal given.

RINGWORM OF THE SMOOTH SKIN

Treatment

Prehn reported the results of treatment of 576 men from 5 ships of the U.S. Navy suffering from mycotic infections of the glabrous skin. In 87 per cent the infection was on the feet, and in 20 per cent of these it was of the pompholyx type and in 5 per cent eczematoid. In 12 per cent the infection was in the thigh-scrotal-anal region (tinea cruris), in 16 of these 69 men there was also infection of the feet, in 2 of the external auditory meatus, and in one of the hands. In 3 per cent of the 576 men erythrasma of the axilla was present. In 2 per cent the hands were infected. Ten men had infection of the external auditory meatus. The incidence of infection fell from 91 per cent to 5 per cent in one month, and to nil in 2 months. They used a powder consisting of salicylic acid, 5 grams; menthol, 2 grams; camphor, 8 grams;

boric acid, 50 grams; and starch, 35 grams. This was rubbed into the skin daily, or more often, and the treatment was continued for several weeks after apparent healing. Loose skin, scales, and the roots of bullae or pustules should be removed, and the powder thoroughly rubbed into the exposed area. As a prophylactic, weekly applications are sufficient. 529-535

RARER INFECTIONS

FAVUS

Manca-Pastorino gave details of a very marked case of favus capitis in which there were also peculiar flat papulo-squamous lesions on the scrotum. The lesions suggested syphilis, psoriasis, or lichen. Microscopic sections of these lesions did not show anything characteristic, and fungus elements could not be demonstrated. All attempts to culture a fungus were negative. But, from the presence in the patient of a positive intradermal reaction to an *Achorion* extract, and the spontaneous disappearance of the lesions when the scalp favus was cured, the author concludes that the scrotal lesions were a peculiar form of favide. 539

DERMATOPHYTIDES

AETIOLOGY AND CLINICAL PICTURE

Erysipelas-like eruptions on the legs not uncommonly accompany active dermatophytosis of the feet. Response to trichophytin and to adequate treatment of foot infection suggest a dermatophytid origin (Sulzberger *et al*). 544

Detection of Fungi

Kesteven devised a new method for staining skin and hairs for the detection of fungi.

The reagent is prepared as follows: to 50 c.cm. each of pure phenol and oil of cloves as much dry picric acid as may be lifted on a threepenny piece (approximately 0·5 g.) is added. When this has dissolved, the reagent is ready. Some of this is poured into a watch glass, and the pieces of skin or hairs are dropped into it and left till cleared completely. This takes from 5 minutes to 2 hours, depending on the thickness of the pieces and the amount of moisture they contain. When cleared, the specimens are transferred to a slide and examined in the reagent under a cover-slip. If desirable to preserve them they can be mounted without further treatment in Canada balsam. This method, under trial for 12 months, had in no instance failed to disclose the presence of fungi in scales from the same source as that in which the mycelium was found by the potassium hydroxide method. On the other hand, it had revealed fungus when the other method failed. Pieces of skin that have been treated with tar or with calomine, or are very sodden, stain better if previously treated with alcohol and ether. Specimens may be left in the reagent for days without deteriorating. Canada balsam mounts after one year are as clear as when made.

Cleveland, D. F. H. (1937) *Canad. med. Ass. J.*, **38**, 38.
Dowding, F. S., and Orr, H. (1937) *Brit. J. Derm.*, **49**, 298.
Emmons, C. W. (1934) *Arch. Derm. Syph., N.Y.*, **30**, 337.
Kesteven, H. L. (1937) *Brit. J. Derm.*, **49**, 500.
Manca-Pastorino, V. (1937) *G. ital. Derm. Sif.*, **78**, 263. Abstracted in *Brit. J. Derm.* (1937) **49**, 516.
Prehn, D. F. (1938) *J. Amer. med. Ass.*, **111**, 685.
Sulzberger, M. B., Rostenberg, A., and Goetze, D. (1937) *J. Amer. med. Ass.*, **108**, 2189.
Torres, F. M. (1936) *Acta dermo-sifilogr., Madr.*, **28**, 754. Abstracted in *Brit. J. Derm.* (1937) **49**, 85.

GALL-BLADDER AND BILE-DUCTS

See also Surveys and Abstracts 1939, pp. 48 and 344.

Prevention of Post-Operative Haemorrhage

The use of vitamin K and bile salts in the prevention of haemorrhage after operations on the gall-bladder is described on pp. 113 and 169. 545-550

GASTRITIS

See Surveys and Abstracts 1939, p. 47. 558

GERMAN MEASLES

559 In the winter of 1935-6 a very wide-spread epidemic of German measles broke out in Quebec and Ontario, affecting probably 100,000 persons, lasting about 6 months, and without any fatality. Cushing summarized the information collected at this time as follows. Second attacks were very rare. The incubation period was always between 2 and 3 weeks, usually 17 days. The causal agent, generally agreed to be a filtrable virus, spread by direct contact from patient to patient, it was difficult for a third person to convey it and carriers were unknown. The infective period was never more than 5 days and infectivity was highest in the pre-eruptive stage. The fever rarely lasted more than 3 days. Adenitis was often present 1 or 2 days before the rash. The rash was quite commonly accompanied by an enanthem on the mucous membrane of the mouth and throat resembling the Koplik spots in measles. Conjunctivitis and stiff joints or arthritis were not infrequent. Complications were few and usually mild, but several cases of encephalitis occurred which, although often leading to convulsions or coma, were of short duration and without any sequelae. Cases of encephalitis or meningo-encephalitis following German measles were described by Adler and by Welch. Read reported one case, in a man aged 26, who recovered. Davison and Friedfeld described 6 cases, 3 of which proved fatal.

Adler, A. (1937) *Hygeia*, **99**, 774.
Cushing, H. B. (1938) *Canad. med. Ass. J.*, **38**, 24.
Davison, C., and Friedfeld, I. (1938) *Amer. J. Dis. Child.*, **55**, 496.
Read, C. I. (1937) *J. Amer. med. Ass.*, **109**, 654.
Welch, A. S. (1938) *J. Mo. med. Ass.*, **35**, 251.

GLANDULAR FEVER

561 See Surveys and Abstracts 1939, p. 348.

GLAUCOMA

562-565 See Surveys and Abstracts, pp. 129 and 349.

GLYCOGEN DISEASE

566 See Surveys and Abstracts, p. 351.

GLYCOSURIA

See also Surveys and Abstracts 1939, p. 352.

DIAGNOSTIC TESTS

Benedict's and Fehling's Tests

567 *Fehling's test.*—In lines 10 and 11 of the paragraph on Fehling's test on page 594 of Vol. V substitute 'potassium' for 'sodium', to read as follows: solution B contains 176 g. of Rochelle salt and 77 g. of potassium hydroxide in water to 500 c.cm.

THE CLINICAL SIGNIFICANCE OF THE REDUCING SUBSTANCES

568 *Laevulosuria.*—For paragraph 3 on page 597 of Vol. V substitute the following: Laevulosuria after a dose of laevulose may occur either (i) because the blood-sugar rises too high, or (ii) because the threshold of the kidney is set at a lower level than usual.

For paragraph 5 on page 597 of Vol. V substitute the following.

(ii) The normal threshold of the kidney for laevulose is set considerably lower than for dextrose, and 'sugar' often appears in the urine when a laevulose tolerance test is performed (Spence and Brett). Laevulosuria sometimes occurs spontaneously in healthy people, especially if they have been eating plenty of fruit. When the nature of the reducing substance is known it is unnecessary to institute any treatment.

Glycuronates.—Vol. V, p. 598, line 11, delete 'glycine as', to read 'combined with glycuronic acid'.

568

Homogentisic acid.—Vol. V, p. 598, last paragraph, 4th sentence, substitute the following: Each drop is followed by a deep purple, or green, or blue colour which disappears at once.

REFERENCES

Substitute the following reference for Harrison, G. A. (1930):

Harrison, G. A. (1937) *Chemical Methods in Clinical Medicine their Application and Interpretation with the Technique of the Simple Tests*, 2nd ed., London, p. 117.

GOITRE AND OTHER DISEASES OF THE THYROID GLAND

See also Surveys and Abstracts 1939, p. 352.

ENDOCRINE INTERRELATIONSHIP IN THYROID DISEASES

569-574

The recent developments in knowledge of goitre and diseases of the thyroid deal mainly with the relation of the thyrotrophic hormone of the anterior lobe of the pituitary gland to the function of the thyroid gland and to exophthalmos.

Thyrotrophic extracts of the anterior pituitary on injection into animals and man cause a rise in basal metabolism and hyperplasia of the thyroid. But even if the injections are continued, the metabolism returns to normal and the gland undergoes involution. Associated with this regression in the activity of the thyroid, it is possible to demonstrate the presence in the serum of the injected animal or man of an action inhibitory to the thyrotrophic extract of the anterior pituitary. It has not been possible to demonstrate the presence of this antithyrotrophic action in the serum of cases of toxic goitre and, although it is accepted that the activity of the thyroid gland is normally under the control of the anterior pituitary, there is no evidence so far that there is excessive anterior pituitary activity in cases of toxic goitre, though the occasional association of toxic goitre with acromegaly is suggestive that such may occur. In a proportion of the animals receiving injections of thyrotrophic extract of the anterior pituitary, exophthalmos is produced. This occurs even in animals from which the thyroid has been removed. Further, in those in whom thyroid hyperplasia and a rise in metabolism have been produced, the exophthalmos occurs in the stage of regression when the metabolism has returned to normal and the gland has undergone involution. The production of exophthalmos is therefore independent of the function of the thyroid and may possibly be enhanced by a diminution in, or absence of, thyroid activity. In cases of toxic goitre, exophthalmos may sometimes arise or increase in severity after subtotal thyroidectomy and it is commonly observed that the degree of exophthalmos is not directly related to the severity of toxicity. These clinical observations are in agreement with the experimental production of exophthalmos in animals receiving thyrotrophic extract of the anterior pituitary. So far, exophthalmos has not been reported as being produced in human beings by injections of such extracts, and although there seems considerable evidence that exophthalmos is the result of anterior pituitary activity rather than of activity of the thyroid, the parts played by disturbances of these glands in the exophthalmos of toxic goitre are not yet clear.

There is evidence that the exophthalmos resulting from injection of thyrotrophic extracts of the anterior pituitary in animals is prevented by division of the cervical sympathetic fibres, and lessened by the administration of thyroxine and of iodine. Sympathectomy has been successfully employed in the treatment of severe exophthalmos in man continuing after subtotal thyroidectomy.

Useful summaries of the recent work and further references are given by Scowen (1937) and Marine (1938).

Marine, D. (1938) *Ann. intern. Med.*, **12**, 443.
Scowen, E. F. (1937) *Lancet*, **2**, 799.

GONORRHOEA

Vol. VI

See also Surveys and Abstracts 1939, pp. 155 and 356.

BACTERIOLOGY

575

The value of cultures in diagnosis is summarized in a leader in the *Journal of the American Medical Association* (1939, Vol. **112**, p. 1158). It quotes Carpenter *et al.* who showed that, of 223 bacteriological examinations reported as positive for

575 gonococci, 91·9 per cent were positive by culture, but only 48 per cent by smear. The use of both methods is therefore indicated.

Stout and Todd found culture superior to smear in 15·6 per cent, but smear superior to culture in about the same percentage. Jacobsen *et al.* also found culture superior to smear.

GONORRHOEA IN MALES

Treatment

General Treatment

576 *Chemotherapy with drugs of sulphonamide group* —The most notable advance in the treatment of gonorrhoea is in the development of treatment by sulphonamide drugs. Many articles have testified to the value of these compounds, but two outstanding questions which are not yet settled are (i) when to begin their use, and (ii) the dosage.

One school advocates waiting until some immunity has developed, say for 8 to 21 days. This is supported by some scientific observations such as those of Fleming, who described experiments illustrating the advantage of combining vaccine or serum therapy with administration of sulphonamides. Those whose reports show an advantage in waiting until some immunity has developed include Dees and Young; Hanschell; Walsh; Cokkinis and McIlligott, Van Slyke *et al.*; Felke; Schreus; Strempel, and Fischer.

As a result of a review of the reports on treatment of 600,000 cases of gonorrhoea with uleron (this preparation is identical with DB 90, mentioned in Vol. VI, p. 17), the manufacturers concluded that the optimal day for beginning the treatment is the tenth.

Probably the majority of authorities would now favour waiting until the eighth day or later when the preparation used is uleron, *p*-aminobenzenesulphonacetamide (albucid), sulphanilamide, or prontosil album, but most users of 2-sulphanilylaminopyridine or Dagenan (M & B 693) think it unnecessary to wait.

Dees and Young reviewed 39 articles relating to 2,727 cases treated with sulphonamide compounds. They concluded that they are valuable but found it difficult to assess results owing to differing standards. They thought that the action of the drug is bacteriostatic, and that gonococci are removed from the body by immune substances. The importance of rigid tests of cure was emphasized.

Cokkinis and McIlligot (1938) reporting on 633 cases (491 male) of gonorrhoea treated principally with *p*-aminobenzenesulphonamide (prontosil album, sulphanilamide) thought that immunity is a factor, and recommended combined treatment with vaccine according to the following technique. The vaccine is started at once and given twice weekly, 5 millions increasing to 100 millions continued throughout the therapy. The sulphanilamide is started 8 to 10 days after the appearance of the discharge, and continued for 3 weeks. The daily dosage is 3 to 5 g., usually 4 g., but varies according to weight. 2 tablets are given after each of the 4 daily meals. After this, tests of cure should be made. The period of observation which they then recommended was about 11 weeks. Later (1939), however, they advanced evidence to show that cases treated with sulphonamide compounds should be observed for a considerably longer period. This view was based on an analysis of 1,268 male and 210 female cases of gonorrhoea the treatment of which had been completed more than six months previously. Of the total male cases 263 had either failed to respond to treatment or defaulted before complete tests, leaving 1,005 who had remained well for more than three weeks after their last treatment. Of these, 12 per cent had relapsed subsequently, this figure must be regarded as minimal as only a relatively small number were under observation after the sixth month, and from then on late relapse cases were still returning. The authors estimated that the percentage of late relapses in their series was between 12 and 27. They stated that late relapses after sulphonamide treatment could easily be distinguished from early relapses and from reinfections (of which there were 100 cases) by their clinical characteristics, the late relapse usually starting quietly and becoming established as a fully purulent urethritis only after a week or so. In their opinion the analysis of their relapses, reproduced in the table below, supported their view that it is better in the long run to delay the start of chemotherapy of gonorrhoea until after the first week of symptoms. They were unable to say if administration of vaccines had affected the relapse rate. Moreover, relapses in a very high proportion of their cases could not be attributed to sub-average dosage. Their figures relating to female cases were to much the same effect.

Showing Early and Late Relapse Rate after Sulphonamide Therapy

Compound	State of Gonorrhoea when Compound Begun	Gross Total of Cases*	Net Total†	Early Relapses‡	Early Relapse Rate	Late Relapses‡	Late Relapse Rate§
Sulphanilamide	1st week –	216 (all Gc. +)	170	53 (all Gc.)	31.2%	20 (16 Gc. +)	12%
	2nd week –	230 (all Gc. +)	196	27 (23 Gc.)	13.8%	12 (9 Gc. +)	6.1%
	3rd week to 12th month –	248 (188 Gc. +)	227	26 (22 Gc. +)	11.5%	10 (5 Gc. +)	4.4%
	After 12th month	66 (25 Gc. +)	57	9 (3 Gc. +)	15.8%	9 (1 Gc. +)	15.8%
Total sulphanilamide cases		760 (659 Gc. +)	650	115 (101 Gc.)	17.7%	51 (31 Gc. +)	7.8%
Sulphapyridine	1st week –	168 (all Gc. +)	128	13 (all Gc.)	10.2%	24 (17 Gc. +)	18.7%
	2nd week –	142 (all Gc.)	112	5 (all Gc.)	4.5%	17 (14 Gc. +)	15%
	After 2nd week Sulphapyridine only	47 (39 Gc. +)	31	1 (Gc. +)	3%	5 (3 Gc. +)	15.1%
	Sulphapyridine after other sulphonamides	51 (26 Gc.)	31	6 (all Gc.)	11.8%	10 (6 Gc.)	32.1%
Total sulphapyridine cases		408 (375 Gc. +)	304	25 (all Gc.)	8.6%	56 (40 Gc.)	18.5%
Uleron	1st and 2nd weeks –	46 (all Gc. +)	26	22 (all Gc.)	84.6%	6 (all Gc. +)	23%
	After 2nd week	54 (34 Gc. +)	34	20 (16 Gc.)	58.8%	5 (1 Gc.)	15%
Total uleron cases –		100 (80 Gc. +)	60	42 (37 Gc. +)	70%	11 (7 Gc.)	18%

* All these are cases of proved gonococcal infection, but cases in which gonococci were seen at the start of chemotherapy are given in brackets

† After deducting early defaulters and failures, and including only cases which passed at least one series of tests and a follow-up of at least three weeks

‡ Cases which relapsed more than once are counted as only one relapse. Relapsed cases in which gonococci were actually seen are shown in brackets, but gonococcal infection was suspected and probably present in most of the others

§ For reasons given in the text these figures are probably considerably below the true relapse rate.

Van Slyke, Thayer, and Mahoney reported on 100 hospital cases, 84 per cent of which were cured. Of the acute cases of less than 28 days' duration, 76·6 per cent were cured; of the chronic cases of more than 28 days' duration 97·2 per cent were cured. An intensive course of 7·77 g. daily for a short period was better than smaller doses for a long period.

Cokkinis reported favourably on sulphonamide preparations in non-gonococcal urethritis.

The use of sulphanilamide in 1,625 male cases of gonorrhoea was reported by Silver and Elliott. Of 200 patients, 58·5 per cent were clear within a month, 21·5 per cent showed less response and needed local treatment. The time required for cure was 45 days. The response in the remainder was relatively unsatisfactory. They gave 5 g. for 2 days, 4 g. for 4 to 5 days, and 1·3 to 2·6 g. for at least 2 weeks. The relation between the duration of disease and success from the treatment was as follows.

Duration	Clear in One Month without Local Treatment	Clear in 8 Weeks with Help of Local Treatment	Unsuccessful Cases
2 days – – –	4	4	2
2–7 days – – –	22	9	9
1–6 weeks – –	53	17	17
6 weeks to 6 months	31	9	10
6 months – – –	7	4	2

These authors considered that the difference was not significant. In gonococcal ophthalmia they obtained brilliant results agreeing with those of Wills.

The following scheme of dosage of uleron is based on the reports of some 600,000 cases. Only irrigations are given until the tenth day of the infection, then uleron, 3 g. daily for 4 days or 4 g. daily for 3 days. If the slide is still positive, the course of uleron is repeated after an interval of not less than 8 days. If progress is still unsatisfactory after the second course, a third may be given after a similar interval. The number of courses should not exceed three.

576 **Strempel considered that the earlier successes with uleron were not sustained when early acute stages of gonorrhoea began to be treated with the drug. He gave details of 264 uncomplicated cases of which 247 were cured with from 1 to 3 courses, and 163 with one such course. a course lasted 3 to 4, or at most 5, days on each of which 3 to 4 g. were given. The interval between courses was presumably one week.**

Hanschell treated 200 cases of gonorrhoea with uleron, 3 g. a day for 5 days, followed by omission of the drug for 2 to 4 days, and then repetition of the course. Most patients needed 3 such courses. Uleron is effective when commenced 5 to 14 days after infection, but even more so in infections of 21 days' duration and over. This superiority of uleron over sulphanilamide, asserted by Hanschell, was contested by McElligott and Cokkinis.

Walsh reported 26 cases treated with uleron. Non-acute cases responded more readily than acute.

The scheme recommended for albucid is: 1st week, urethral irrigation thrice daily and injections of vaccine; 2nd week, 3 tablets (1·5 g.) albucid 3 times a day, continuing the irrigation; 3rd week, no treatment unless the discharge has not stopped, in which case irrigation is given; 4th week, tests of cure are started if the discharge ceased at the end of the first week: if it did not do so, the course of albucid is repeated.

Using Dagenan (M & B 693) the course recommended by Lloyd, Erskine, and Johnson (1938*b*) is, 2 g. a day for 5 days, 1·5 g. a day for 5 days, and irrigation. Marinkovitch recommends 3 g. a day for 3 weeks. Batchelor *et al.* recommend 3 g. a day for 5 days, and 1·5 g. a day for 5 to 9 days.

Lloyd *et al.* (1938*a*) in a preliminary report on the effect of M & B 693 on 36 adults and 7 children, obtained good results but reported toxic effects in 10 adults. They later reported on 250 cases of gonorrhoea treated with M & B 693, 108 being acute uncomplicated cases with discharge of not more than a week. The results were superior to those with sulphanilamide.

Bowie reported on 30 cases treated with M & B 693. The duration of infection at the start of treatment was not believed to be a factor. He reported an excellent result in a case of ophthalmia neonatorum after failure with prontosil. The dosage was 0·25 g. thrice daily. Since publication of this paper Bowie, Anderson, Dawson, and Mackay have published one in which, after describing results in 104 cases of gonorrhoea treated with M & B 693, they reported on 23 treated more intensively than the above, namely with 8 tablets (4 g.) at once, 4 in 4 hours, and thereafter 2 every 4 waking hours until the end of a period of approximately 72 hours from the beginning of treatment. The incidence of toxic reactions was high (78 per cent), but only 22 per cent of the cases were severe and symptoms were present only during the first 24 hours of treatment. The authors suggested that major or dangerous toxic effects are more likely to arise from prolonged than from brief treatment. Of the 23 cases, 20 were cured, one was probably cured, and in 2 the result was doubtful.

Marinkovitch treated 100 male cases with prontosil album starting at once, 50 with uleron, starting after a delay of 14 days, and 50 with M & B 693. The dosage was 3 g. a day for 3 weeks, plus lavage. He expressed the view that M & B 693 is much superior to prontosil album and uleron.

Toxic effects.—The reports on the sulphonamide compounds appear to show that all give rise to much the same kinds of toxic effect. Perhaps M & B 693 is a little more toxic than prontosil and sulphanilamide, and these than uleron. Uleron, although less toxic on the whole, appears to be peculiar in being liable to give rise to peripheral neuritis when the dosage is pushed.

The toxic effects of drugs of the sulphonamide group are described in detail on page 176.

Wendel reported that in Washington University School of Medicine, Hartmann injected 1 mg. of methylene blue per kg. body-weight into two children showing moderate cyanosis and methaemoglobinaemia, and that the methaemoglobinaemia was reduced from 20 per cent to 3 per cent in 45 minutes in one patient and from 18 per cent to less than 3 per cent in the same time in another. Methylene blue had been used previously by Williams and Challis as an antidote in *p*-bromaniline poisoning, and later Steele and Spink used it with dramatic results in aniline poisoning and in acetanilide poisoning—one case each.

Fever treatment.—A report by Krusen and Elkins on fever therapy by physical means, authorized by the Council on Physical Therapy of the American Medical Association, states that the results obtained in over 1,000 cases of gonorrhoea

treated by physically-induced fever show conclusively the value of this method. Approximately 90 per cent of the cases showed remissions. A satisfactory procedure is to maintain a temperature between 106 and 107 F. (41·1 to 41·7 C.) for 10 hours; a single such session causes remission in the great majority of cases. 576

For patients who cannot tolerate sulphanilamide, or in whom the drug does not eradicate the infection, a combination of the drug and hyperpyrexia has proved most efficacious.

Tests of Cure

Gonococcal complement-fixation test.—An article by Hayden and Hayden presents evidence that infection with *Meningococcus*, Group 2, may give rise to a positive reaction with the gonococcal complement-fixation test. The same authors point out the narrow margin between the amount of fixation by the antigen in Price's method and that permitted to rank as positive.

Tests in sulphonamide treatment.—Most investigators emphasize the importance of stringent tests of cure, as sulphonamide treatment, when it fails, is apt to result in a rather long period of clinical latency which may give the impression that the patient is cured.

GONORRHOEA IN ADULT FEMALES

Clinical Picture

Superior Right Abdominal Complex in Gonococcal Adnexitis

Mauro recalls that Curtis frequently noted adhesions in the superior right quadrant of the abdomen between the parietal peritoneum and the anterior surface of the liver, and called them violin-string adhesions. Fitz Hugh proved one case to be gonococcal by bacteriological tests. The case was one of very acute hepatic colic calling for surgical intervention. No gall-bladder or other disorders were found other than inflammation of the peritoneal covering of the anterior face of the liver and the parietal and diaphragmatic surfaces adjoining it. The patient had a gonococcal adnexitis. According to Mauro, Florian and Claudian (1938) studied many such cases, and found in nearly all a serous effusion in the right pleural cavity. 577

Mauro says that he has often noted the frequency with which sufferers from salpingitis complain of pain in the right superior quadrant, where adhesions are often found. He reports a case after a curettage for a miscarriage. The front of the liver in the duodeno-gastric furrows was covered with many deposits of fibrin, the stomach and duodenum were not altered. The trumpets of the tubes were very hyperaemic and covered by a suspicious serosity containing gonococci. On the eighth day the upper wound broke and dense pus containing gonococci escaped.

Mauro gives the following account of such cases of gonococcal perihepatitis. In a woman with salpingitis, under the influence of gynaecological manœuvres or apparently spontaneously, a syndrome develops, localized in the right hypochondrium, or sometimes in the left; there is pain radiating also to the epigastric region, the subscapular, and the right shoulder with abdominal muscular rigidity and cutaneous hyperaesthesia. In the right pleural *cul-de-sac* signs of inflammation are found, sometimes with a serous effusion. Some general symptoms such as gastric pains and vomiting also occur. There is not much fever. Jaundice is rare. He discusses the possible routes of spread, and considers that dissemination by the blood-vessels is unlikely, the possibility of lymphatic spread is interesting but does not explain all cases; he considers direct spread along the parietal peritoneum to be the most likely.

Pericholecystitis

In 1934 Holler and Mahrycostas of Vienna reported 18 cases of pericholecystitis of gonococcal origin.

Treatment

Acute Gonorrhoea

For women, Cokkinis and McElligott recommend a vaccine as in men. Sulphanilamide treatment is not begun until the eighth day and is continued for 3 weeks. The dosage is 3 g. a day. Tests of cure are instituted at the end of 3 weeks. Examination is repeated fortnightly for one month, and then monthly for two months.

VULVO-VAGINITIS IN CHILDREN

Prevention.—The London County Council has published a valuable report by a Departmental Committee on Vulvo-vaginitis in Children. 578

Treatment

Oestrogenic Hormones

578 Te Linde reported good results from insertion of one pessary of amniotin containing 1,000 units each night for 2 weeks.

Sulphonamide drugs.— In vulvo-vaginitis, Brown demonstrated good results with M & B 693 in 27 girls, between the ages of 3 and 10. The majority of cases had 0·25 g. 4 times daily, after food and at bed-time for 4 days. The only local treatment was swabbing the vulva with acriflavine, 1 in 1,000 parts of glycerin, and dusting with dermatol (bismuth subgallate) powder. With two exceptions all were negative for gonococci in 2 to 7 days. Acute inflammation with purulent discharge cleared up rapidly, sometimes after the second dose

Of the two exceptions, one was a failure, and one cleared up by the eighth day. Besides the one failure, one patient relapsed twice but remained negative after a third course. Of the 25 remaining cases which received one course, 14 were discharged and under observation at other clinics, 3 had required more treatment.

Prontosil album was not so good as M & B 693, which cured in a shorter time and required no local treatment Ulcron acted more slowly than either of these two. The author compares sulphonamide therapy of vulvo-vaginitis with other forms of treatment, such as painting and oestrin. With painting, the average duration of treatment of 156 cases was 17 weeks; under oestrin (36 cases) 3 to 12 weeks; under prontosil album (31 cases) 10 to 21 days, and under M & B 693 (27 cases) 4 days.

Batchelor, R. C. L., Lees, R., Murrell, M., and Braine, G. I. H. (1938) *Brit. med. J.*, **2**, 1142
Boller, R., and Mahrycostas, K. (1934) *Klin. Wschr.*, **13**, 1180.
Bowie, I. J. I. (1938) *Brit. med. J.*, **2**, 283.
Anderson, T. L., Dawson, A., and Mackay, J. F. (1939) *Brit. med. J.*, **1**, 711.
Brown, D. K. (1939) *Brit. med. J.*, **1**, 320
Carpenter, C. M., Leahy, A. D., and Wilson, K. M. (1938) *Amer. J. Syph.*, **22**, 55
Claudian, L., and Florian, I. (1938) *Ann. Méd.*, **43**, 62.
Cokkinis, A. J., and McElligott, G. L. M. (1938) *Lancet*, **2**, 355.
Curtis, A. H. (1930) *J. Amer. med. Ass.*, **94**, 1221.
Dees, J. E., and Young, H. H. (1939) *Vener. Dis. Inform.*, **20**, 33.
Eelke, H. (1937) *Munch. med. Wschr.*, **84**, 1867.
Fischer, C. (1937) *Fortschr. Ther.*, **13**, 553
Fitz Hugh, T., Jnr. (1934) *J. Amer. med. Ass.*, **102**, 2094.
Fleming, A. (1939) *Brit. med. J.*, **1**, 688
Hanschell, H. M. (1938) *Brit. med. J.*, **2**, 375
Hayden, A. F., and Hayden, A. F. (1939) *Brit. J. vener. Dis.*, **15**, 45.
Jacobsen, E., Mason, H. C., and Arnold, L. (1938) *J. Lab. clin. Med.*, **23**, 729.
Krusen, F. H., and Elkins, I. C. (1939) *J. Amer. med. Ass.*, **112**, 1689
Lloyd, V. L., Erskine, D., and Johnson, A. G. (1938 a) *Lancet*, **1**, 1305.
(1938 b) *ibid.*, **2**, 1160
London County Council (1938) Report of Departmental Committee on 'The Clinical and Administrative Aspects of Vulvo-vaginitis in Children'. Abstracted in *Brit. med. J.* (1938) **2**, 961.
McElligott, G. L. M., and Cokkinis, A. J. (1938) *Brit. med. J.*, **2**, 424.
Mauro, F. (1938) *Pr. méd.*, **46**, 1919.
Marinkovitch, R. (1939) *Brit. med. J.*, **1**, 317.
Schreus, H. T. (1937) *Arzt f. Rheuml.*, Heft 24, 294.
(1937) *Derm. Z.*, **76**, 253.
Silver, B., and Elliott, M. (1939) *J. Amer. med. Ass.*, **112**, 723.
Steele, C. W., and Spink, W. W. (1933) *New Engl. J. Med.*, **208**, 1152.
Stuut, B. F., and Todd, D. A. (1938) *Tex. St. J. Med.*, **34**, 211.
Strempel, R. (1939) *Med. Welt*, **13**, 217.
Te Linde, R. W. (1938) *J. Amer. med. Ass.*, **110**, 1633.
Van Slyke, C. J., Thayer, J. D., and Mahoney, J. F. (1937) *Vener. Dis. Inform.*, **18**, 417.
Walsh, D. F. (1938) *Brit. med. J.*, **2**, 215.

Wendel, W. B. (1937) *J. Amer. med. Ass.*, **109**, 1216.
Williams, J. R., and Challis, F. E. (1933) *J. Lab. clin. Med.*, **19**, 166.
Willis, T. (1938) *Yale J. Biol. Med.*, **10**, 275.

GOUT

See also Surveys and Abstracts 1939, p. 359.

PATHOLOGY

579 The view that impairment of the power of the kidney to excrete uric acid is the chief causal factor in gout has been modified as a result of the work of Folin and his collaborators. From this it appears that gouty patients are able to excrete uric acid injected into them as rapidly and completely as normal controls. Moreover, gouty persons can, in the early stages, concentrate uric acid in their urine to as high a level as normal individuals. The view of Folin *et al.* that increased formation of uric acid was of more importance than diminished excretion has received the support of Talbott and Coombs, as the result of their metabolic studies on 24 patients with gout.

Vol. VI, on page 39, 5th paragraph. The statement that uric acid is generally present in the blood in organic combination with thymine acid is now open to question.

CLINICAL PICTURE

The occasional association of gout with infective arthritis should be noted.

TREATMENT

General and Spa Treatment

According to Buckley, colchicum remains the most effective remedy. It does not appear to affect the excretion of urates, and might be combined with sodium salicylate, which has such an effect. Inclusion of sufficient alkali to keep the urine alkaline and thus prevent deposition of uric acid in the urinary tract is advisable as in the following prescription

Colchicum wine	15 minims
Sodium salicylate	20 grains
Potassium bicarbonate	30 grains
Liquid extract of liquorice	10 minims
Peppermint water to	1 ounce

This dose might be repeated in an hour and continued at intervals of 2 or 3 hours until symptoms became less acute; the interval might then be increased 3 times a day, and this dosage continued until the attack has subsided or symptoms of overdosage, such as nausea or diarrhoea, occur

Buckley, C. W. (1938) *Med. Pr.*, **197**, 482.
Folin, O., Berglund, H., and Denick, C. (1924) *J. biol. Chem.*, **60**, 361.
Talbott, J. H., and Coombs, F. S. (1938) *J. Amer. med. Ass.*, **110**, 1977.

GRANULOMA, ULCERATIVE

AETIOLOGY

580 Dienst, Greenblatt, and Sanderson inoculated a volunteer negro subcutaneously in the region of the groin with a bacteria-free exudate rich in Donovan bodies. A typical lesion was produced, in the exudate from which there were monocytes containing aggregates of Donovan bodies.

DIAGNOSIS

Greenblatt, Torpin, and Pund reported that out of 45 cases of ulcerative granuloma 2 were extra-genital; their review of the literature showed that about 6 per cent of all cases are extragenital. They insist that the presence of Donovan bodies is essential for diagnosis; these organisms may not appear in smears, and biopsy may be necessary for their demonstration.

TREATMENT

Ross treated a case seen in Liverpool, but in which the disease had been contracted a month previously in Brazil, with M & B 693; no other general treatment was

580 employed; six tablets, each of 0·5 gram, were given daily for 14 days, and immediate improvement followed. In 5 days the ulceration was half healed; in 10 days epithelialization was in an advanced state, in 14 days was complete, and during the subsequent 11 days there was not any recurrence

Dienst, R. B., Greenblatt, R. B., and Sanderson, F. S. (1938) *J. infect. Dis.*, **62**, 112
Greenblatt, R. B., Torpin, R., and Pund, I. R. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 358
Ross, A. O. F. (1939) *Lancet*, **1**, 26.

HAEMATEMESIS

582 See Surveys and Abstracts 1939, pp. 4[illegible] and 360

HAEMATOPORPHYRINURIA

583, 584 See Surveys and Abstracts 1939, p. 361

HAEMATURIA

585-586 See Surveys and Abstracts 1939, p. 361

HAEMOGLOBINURIA

CLINICAL PICTURE

Haemoglobinuria due to Chemical Agents

Sulphonamide Compounds

589 Kohn recorded the case of a child, aged 1 year, with acute otitis media, who after 12 doses of 0·3 gram (5 grains) each of sulphanilamide 3 times a day, developed haemoglobinuria which disappeared when the drug was discontinued. Strasser and Singer report another case in a patient 36 years old who was given prontosil rubrum for a sore throat occurring 7 days after appendicectomy. After 8 tablets had been taken haemoglobinuria appeared, the prontosil was stopped and the haemoglobinuria disappeared in 3 days.

Paroxysmal Haemoglobinurias

Cold Haemoglobinuria

592 *Ascorbic acid.* Pfeiffer and Arnove investigated on white rats the effect of vitamin C on paroxysmal haemoglobinuria produced by subcutaneous administration of glycerin; administration of ascorbic acid before the injection of glycerin raised the dose necessary to produce haemoglobinuria by 100 per cent or more. Armentano discovered C-hypovitaminosis in a patient with paroxysmal (cold) haemoglobinuria. After treatment for several days with 300 mg. ascorbic acid the haemoglobinuria disappeared. The protective action of ascorbic acid on red blood cells can be demonstrated *in vitro*.

Haemolysin. Anaemia with Haemoglobinuria

Marchiafava-Micheli type. Ham reported 5 cases of this syndrome. In 2 an increase in haemoglobinaemia occurred during sleep whether by day or by night, the third patient, whose spleen had been removed, did not show this feature. During sleep the *p*H of the blood falls, red cells are abnormally susceptible to haemolysis both *in vivo* and *in vitro* in plasma of increased acidity within a physiological range of *p*H variation. The oral administration of acid-forming salts increases the intravascular haemolysis, and vice versa.

In two further cases, with necropsies recorded by Scott *et al.* outstanding features were thrombosis of the central veins of the liver, siderosis of the renal tubules, and erythroblastic hyperplasia of the bone marrow.

Paroxysmal Haemoglobinuria (Paroxysmal Myoglobinuria)

Three further cases have been recorded. Hubert *et al.* described a case of unknown aetiology in a child, aged 4 years, lasting a few days only and without any sequels; in the subsequent discussion, Debre recalled the 4 cases of this malady previously recorded: one in a child of 13 years, a second in a woman of 38, a third in a woman of 42, and a fourth in a child of 2½ years.

Armentano, I. (1936) *Nature, Lond.*, **137**, 910.
Ham, T. H. (1937) *New Engl. J. Med.*, **217**, 915.

Huber, J., Florand, J., Lièvre, J.-A., and Néret (1938) *Bull. Soc. méd. Hôp. Paris*, **54**, 725. 592
Kohn, S. E. (1937) *J. Amer. med. Ass.*, **109**, 1005.
Pfeiffer, C., and Arnove, I. (1937) *Proc. Soc. exp. Biol., N.Y.*, **37**, 467.
Scott, R. B., Robb-Smith, A. H. T., and Scowen, E. F. (1938) *Quart. J. Med.*, N.S. **7**, 95.
Strasser, A., and Singer, K. (1938) *Med. Klinik*, **34**, 783.

HAEMOPHILIA

See Surveys and Abstracts 1939, p. 361. 594

HAEMOPTYSIS

See also Surveys and Abstracts 1939, p. 362.

TREATMENT

595 At the twentieth annual meeting of the American Association for Thoracic Surgery, 1937, Hoesser discussed control of haemorrhage in pulmonary tuberculosis. There were 2 possible lines of attack. (i) If an aneurysm on a branch of the pulmonary artery, or a tuberculous erosion was responsible for haemoptysis, ligation of a lobar branch at the hilum according to the technique of Sauerbruch should arrest it. (ii) If, however, the leakage was from vessels of the greater circulation (bronchial artery), ligation of the pulmonary vessels could not have any effect, but bleeding could be controlled by mass ligature around the lobar hilum, sufficiently tight to interrupt both the pulmonary and bronchial arteries but not to occlude the bronchus. This will not lead to necrosis and sloughing of the lobe. It had been shown that the nutritional requirements of the pulmonary parenchyma were very modest and enough blood reached the lung via pleuritic adhesions to meet its nutritional needs. The operative results were very disappointing. Of 7 patients treated by intrapleural operations 5 died, the 3 who were treated with hilar ligature all died.

Hoesser, F. (1938) *J. thorac. Surg.*, **7**, 671.

HAEMORRHAGIC DISEASES

See Surveys and Abstracts 1939, p. 362 596-603

HAIR FOLLICLES, ABNORMALITIES AND DISEASES

See Surveys and Abstracts 1939, p. 363 605-612

HEADACHE

See also Surveys and Abstracts 1939, p. 363.

AETIOLOGY

618 Northfield investigated the causes of headache, particularly when associated with intracranial tumours; in 36 out of 100 cases of intracranial tumour headache appeared before, or at the same time as, other complaints, in 9 cases of acoustic tumour in this series headache was not the first symptom. His observations did not support the hypothesis that the headache associated with tumours was due to raised intracranial pressure. In 39 out of 102 verified cases of tumour the pressure of the cerebrospinal fluid was under 200 mm. and in 16 below 100 mm. Many of these patients with normal or subnormal pressure had experienced severe headache immediately before the investigation, on the other hand headache was sometimes absent when the pressure was high. The author considered that a sudden alteration of intracranial pressure, either increase or decrease, was much more probably a cause of headache than raised pressure. He also considered that it was not justifiable to attribute headache to sensitivity of the dura mater. Experiments performed during cerebellar explorations showed that to produce pain by stimulation of the dura, very considerable traction was necessary. The author concluded that headache in cranial tumour was due to an abnormal state of tension in the walls of the cerebral

618 blood vessels, and recalled the fact that intracranial aneurysm caused unilateral headache even when too small to cause an increase in the intracranial pressure. The headache caused by histamine and occurring with a falling intracranial pressure was also explained by a state of abnormal tension in the walls of the cerebral vessels during the period of recovery from the conditions caused by the histamine: namely general vasodilatation and decreased cerebral intravascular pressure and consequent increased intracranial extravascular pressure. The author was able to produce headache experimentally by various means but was not so easily able to relieve it

Northfield, D. W. C. (1938) *Brain*, **61**, 133

HEART DISEASES: I.—CONGENITAL DISEASES

619-635 See Surveys and Abstracts 1939, p. 364.

HEART DISEASES: II.—RHEUMATIC HEART DISEASES IN CHILDREN

636 See Surveys and Abstracts 1939, p. 365

HEART DISEASES: III.—PERICARDIUM DISEASES

637 See Surveys and Abstracts 1939, pp. 58, 60, and 365.

HEART DISEASES: IV.—MYOCARDIUM DISEASES

638-641 See Surveys and Abstracts 1939, p. 367.

HEART DISEASES: VI.—ENDOCARDITIS, MALIGNANT

641-646 See Surveys and Abstracts 1939, p. 368.

HEART DISEASES: VII.—MITRAL VALVE DISEASES

647-651 See Surveys and Abstracts 1939, p. 369

HEART DISEASES: VIII.—AORTIC VALVE DISEASES

652 See Surveys and Abstracts 1939, p. 370.

HEART DISEASES: IX.—RIGHT SIDE DISEASES

HYPERTROPHY

Diagnosis

654 According to Wood and Selzer the tall spiked P wave in the electrocardiograph, which is generally associated with tricuspid stenosis, congenital pulmonary stenosis, and cor pulmonale, may indicate hypertrophy of the right auricle.

Wood, P., and Selzer, A. (1939) *Brit. Heart J.*, **1**, 81.

HEART DISEASES: X.—HEART FAILURE

See also Surveys and Abstracts 1939, pp. 59 and 370.

CLINICAL TYPES

Congestive Heart Failure

659 *Aetiology.* Congestive heart failure with normal rhythm is not uncommon in rheumatic heart disease complicated by pregnancy (Bramwell and Longson).

Signs of ventricular failure. Acute failure of both right and left ventricles is seen in vitamin B_1 deficiency due to chronic alcoholism (Jones and Bramwell).

TREATMENT

Drugs

Gavey and Parkinson, in a recent investigation, showed that digitalis is useful in the treatment of heart failure with normal rhythm. In fact, if cases of auricular fibrillation due to rheumatic heart disease are excluded, digitalis gives equally good results in normal rhythm and in auricular fibrillation. 659

Bramwell, C., and Longson, E. A. (1938) *Heart Disease and Pregnancy*, London.
Gavey, C. J., and Parkinson, J. (1939) *Brit. Heart J.*, **1**, 27.
Jones, A. M., and Bramwell, C. (1939) *Brit. Heart J.*, **1**, 187.

HEAT-STROKE AND HEAT-EXHAUSTION

AETIOLOGY

Signs of heat-stroke may occur apart from tropical and industrial conditions. Anaesthetic convulsions have been ascribed to heat-stroke. The effect of athletic performances was described in a bulletin of the Health Organisation of the League of Nations (1934) 661

Pyretotherapy may also produce symptoms due to heat-effects. Kopp and Solomon gave a detailed account of symptoms in 8 patients (2 of whom died) undergoing pyretotherapy induced by the Kettering hypertherm which, by exposing the patient to a current of hot moist air, raises the temperature to between 104 and 106° F.; these symptoms were ascribed to shock, disturbances in the circulatory and neurogenic mechanisms, dehydration, alkalosis, hypochloraemia and, at necropsy, degenerative changes in the adrenal cortex. Working in gas-protective clothing, especially in tropical climates, has also been stated to produce discomfort and distress. Sorley experimentally investigated the possibilities of performing continued physical exertion wearing gas-protective clothing in the tropical climate of Singapore, and found that there was not any danger of heat exhaustion if the protective suit was kept continually wet. Hill, working in London, found that wetting the outer surface of the suit did not in his subject relieve the discomfort, and considered that the best index of approaching danger from heat-stroke under these conditions was given by the pulse-rate, which should not be allowed to rise above 140.

With the object of elucidating the effects of high temperature Marsh experimented in Iran on hares and rabbits, which do not perspire, and concluded that in rabbits in a very hot environment a rise of temperature is inevitable, that, when a high brain temperature is reached, the prognosis depends upon its duration, and therefore in all cases of hyperthermia reduction of the temperature should be effected as an emergency measure, and that acclimatization plays a large part in the ability to withstand high temperatures. His paper emphasized the importance of anoxaemia and circulatory failure, factors which are confirmed by Kopp and Solomon.

Canny and Martin investigated the physical laws governing the heat-loss from a cylindrical moist body, and the effect of wind velocity on the evaporative and convective loss. They calculated that variations in the temperature of the dry bulb while the wet bulb temperature is constant have only a slight influence on the heat-loss from the moist cylinder.

PATHOLOGY AND MORBID ANATOMY

Blood Chemistry

Chakravarti and Tyagi analysed the chemical and physical changes in the blood and urine of 10 patients suffering from 'effects of heat', and correlated them with the meteorological data. They found a tendency to retention of non-protein nitrogen, and other indications of renal insufficiency; the loss of chlorides in the sweat was not estimated, as it is stated that sweating is not a feature of heat-stroke, though this is difficult to explain, they found the blood chlorides were reduced in spite of low urinary chloride; the blood lactic acid and other anions were increased.

Gibson and Kopp found that in artificially induced fever there is a diminution in the volume of the circulating blood caused by loss from the skin and lungs. The volume cannot be restored by oral ingestion of fluids, but can be maintained at the prefebrile level by intravenous administration. The prevention of shock was considered to depend on the maintenance of the blood volume.

CLINICAL PICTURE

661 Ferris *et al.* described the clinical and chemical observations on 44 fatal cases of heat-stroke when the environmental temperature was above the normal body temperature. Cessation of sweating usually precipitated the onset of symptoms. Senility and consumption of alcohol were disposing factors.

McCance (1938, a) found that experimental salt-deficiency in man causes reduction in the extracellular fluids, but no constant change in the chloride content of resting saliva and gastric juice; there was a fall in sodium and a rise in potassium in these 2 fluids, a reduction in sodium and chloride in the cerebrospinal fluid, and in the amount of sodium and chloride in the sweat; the latter was more marked in some subjects than in others.

McCance (1938, b) suggests that the difference between individuals in their tolerance of hot climates may be associated with individual differences in the amount of sodium chloride lost in the sweat. In a series of laboratory experiments on human subjects he found that some subjects cannot be rendered deficient in chloride by repeated sweats because after a time almost no sodium chloride is excreted, some, on the other hand, continue to lose considerable amounts and would be likely to suffer in a hot climate unless an adequate intake of sodium chloride was provided.

Further information on physiological studies of high temperature conditions are given by Dill. Recent reports concerning the temperature problem as it concerns work in mines are also given below. The statement in Vol. VI, p. 405, that air-conditioning is not practised in the Witwatersrand gold mines was incorrect.

Annual Report (1936) *Central Mining-Rand Mines Group Health Department*, p. 7.
Canny, A. J., and Martin, C. J. (1939) *J. Hyg., Camb.*, **39**, 60.
Chakravarti, D. N., and Tyagi, N. (1938) *Indian J. med. Res.*, **25**, 791.
Christensen, E. H. (1934) *Quart. Bull. Hlth Org. League of Nations*, Vol. **3**, No. 3, p. 388.
Dill, D. B. (1938) *Life, Heat, and Altitude. Physiological Effects of Hot Climates and Great Heights*, London.
Dreosti, A. O. (1937) *S. Afr. J. med. Sci.*, **2**, 29.
Ferris, E. B., Jnr., Blankenhorn, M. A., Robinson, H. W., and Cullen, G. E. (1938) *J. clin. Invest.*, **17**, 249.
Gibson, J. G., Jnr., and Kopp, I. (1938) *J. clin. Invest.*, **17**, 219.
Hill, L. (1939) *Brit. med. J.*, **1**, 533.
Kopp, I., and Solomon, H. C. (1937) *Arch. intern. Med.*, **60**, 597.
McCance, R. A. (1938, a) *J. Physiol.*, **92**, 208.
(1938, b) *Lancet*, **2**, 190.
Marsh, E. (1938) *Trans. R. Soc. trop. Med. Hyg.*, **32**, 371.
Sorley, E. R. (1939) *Brit. med. J.*, **1**, 385.

HEPATO-LENTICULAR DEGENERATION

666 See Surveys and Abstracts 1939, p. 372.

HERNIA

See also Surveys and Abstracts 1939, p. 372.

EXTERNAL ABDOMINAL HERNIA

Treatment

Operation

673 It is suggested that when operations for double inguinal hernia are carried out simultaneously there is a greater risk of recurrence than when they are operated upon separately.

As bearing on the impression in the profession that the operations for the radical cure of hernia do not give such good results as were supposed, it is essential that cases should be considered in age groups: young adults 18 to 30 give much better results than the group 30 to 50, and so on. The operation should be carried out with great care and these patients should not be handed over to dressers or other inexperienced persons.

Injection
There are not yet any reliable statistics by which the real value of the injection treatment can be assessed. It has the one great advantage that it can be used as an ambulatory method. 673

Sutures
In most cases the use of fascial sutures is only an adjunct, but when tissues are poor (soft and flabby) or the parts cannot be apposed without tension, or the operation is for a recurrence, fascial sutures are probably essential to give the best chance of success.

HERPES

See Surveys and Abstracts 1939, p. 373. 688, 689

HODGKIN'S DISEASE

See also Surveys and Abstracts 1939, p. 375.

MORBID ANATOMY

G. T. Harrell recorded a case with 2 rare lesions of Hodgkin's disease, namely, invasion of the pericardium and of the gall-bladder. He collected 9 cases of invasion of the pericardium, and 2 of pressure by enlarged glands on the extra-hepatic bile-ducts, but regarded invasion of the gall-bladder as unique. 691

CLINICAL PICTURE

Intrathoracic. Wright divided 60 cases of Hodgkin's disease with intrathoracic lesions into 4 groups: (i) enlargement of the mediastinal glands, (ii) involvement of the parenchyma of the lungs, (iii) involvement of the pleurae, (iv) combinations of the above. In 57 cases enlarged mediastinal glands were shown by X-rays. Parenchymatous lesions of the lungs were present in 21 patients, and in 18 of these the mediastinal lymphatic glands were also enlarged. 3 patients showed parenchymatous lesions without involvement of the mediastinal lymphatic glands. Pleural effusion was present in 17 patients all with enlargement of the mediastinum; in 7 cases pleural effusion was associated with enlarged mediastinal glands. In 54 cases superficial glands were enlarged. Intestinal perforation occurred in 2 cases, and jaundice was noted in 2 cases. In 45 cases traced to a fatal termination the average duration of the disease was 40 months. The shortest duration was 7 weeks. Reference was made to a case, not included in the series of 60, in which the disease lasted 26 years, and on 3 occasions high voltage X-ray treatment was life-saving.

Retroperitoneal. In a paper on the symptoms due to involvement of retroperitoneal lymphatic glands A. U. Desjardins drew special attention to those occurring in Hodgkin's disease or lymphosarcoma, for he definitely stated that clinically it was impossible to distinguish between them, and that microscopically there were sometimes serious difficulties. The symptoms often vary from time to time. Although the usual duration of life after the onset was 2 or 3 years, patients might survive 5, 10, 15, or 20 years; but involvement of the para-aortic glands rendered the prognosis worse. The commonest symptoms were loss of weight and strength, a feeling of heaviness in the epigastrium rather than pain (but there might be pain), backache, flatulence, and belching. Fever of the Pel-Ebstein type occurred both in Hodgkin's disease and in lymphosarcoma when involving the retroperitoneal or the mediastinal lymphatic glands; pruritus was present in about the same proportion of cases as fever, but the two were not related, although they might occur together. Increased pigmentation of the skin was another sign that the retroperitoneal glands were lymphadenomatous, and irradiation of the abdomen would diminish this pigmentation. Other symptoms that might occur were constipation or diarrhoea, oedema, ascites, and jaundice. To examine the abdomen for enlargement of the retroperitoneal lymphatic glands, the patient should be in the recumbent position with the head slightly flexed on the chest, the thighs flexed on the trunk, and the upper extremities at the side of the body. The spleen and liver might be enlarged either as part of Hodgkin's disease or independently. Usually radiological examination of the gastro-intestinal tract was negative, but sometimes a filling defect was permanent in the caecum. Occasionally radiological examination of the spine showed destruction of one or more of the dorsal or lumbar vertebrae.

COURSE AND PROGNOSIS

691 **Baker and Mann analysed 65 cases of Hodgkin's disease seen at Guy's Hospital between October 1926 and October 1937, all but one of which were confirmed either by biopsy or by necropsy. Of the 65 cases 47 were males and 18 females; the ages were between 7 and 67, the maximum incidence being in the second and third decades. Half the patients died within 2 years of the first symptoms, the extremes in this duration being one month and 17 years, and the average expectation of life being estimated at 18 months. In all but 4 cases the superficial lymphatic glands were involved and in all but 3 cases from the onset. In 54, or 83 per cent, the cervical lymphatic glands were affected. Hodgkin's disease very rarely occurred primarily in the lungs, the involvement being nearly always secondary to disease of the mediastinal glands. The following classification was suggested: A. The involved mediastinal glands compressing or even causing collapse of the lungs without infiltrating them; this was usually bilateral, but when unilateral the right side was generally affected. B. Lung involvement: (i) diffuse peribronchial spread, (ii) massive lung involvement; and (iii) discrete nodular involvement. C. Pleural involvement: (i) deposits in the pleura, in 3 cases, found after death, (ii) with effusion, in 3 cases. Lung involvement occurred in 30 cases, in 5 of which the mediastinal glands were not affected. The spleen was clinically enlarged in 35 and the liver in 20 cases. In none of the 65 cases were lesions of the alimentary tract apparent. There were 8 cases of disease of the central nervous system, 2 being fatal from paraplegia, one of them after laminectomy which showed epidural masses of lymphadenoma. The blood showed a polymorphonuclear leucocytosis (more than 8,400 polymorphonuclears per c.mm.) in 16 cases, or 28 per cent, and a leucopenia (less than 3,000 white cells per c.mm.) on 4 occasions only. Eosinophilia (5 per cent or more) was noted in 11, or 20 per cent of the cases. In 23 cases, or 41 per cent, the haemoglobin was at some time during the course of the disease below 60 per cent. In all cases in which the disease is clearly limited to peripheral and accessible glands surgical removal, followed by regular X-ray exposures, is advocated. Of 4 cases so treated 2 were stated to be cured.**

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Gordon's test.—Much work has been directed to the investigation of the encephalitogenic agent described in Vol. VI, p. 532. Many authors (e.g. King, McNaught) consider that the agent which gives a positive encephalitic response is associated with the eosinophil cells in the affected glands. That this is not the case is shown by the fact that a positive result is obtained from atypical glands in which no eosinophils can be seen in section, it is, in fact, in these cases that the test is of value. In typical cases the diagnosis can be based on the histological appearances of sections, but, in atypical cases in which eosinophils are absent, but which contain doubtful giant cells with fibrosis—perhaps of minor degree—the biological test is necessary. Gordon's experience is that a positive test has always indicated Hodgkin's disease, whatever the histological diagnosis. Van Rooyen also stressed this.

The nature of this agent has been investigated by Edward, and its action on the central nervous system by Gaupp, in his contribution to a combined paper on Hodgkin's disease, by Uhlenhuth, Wurm, Liebegott, and Gaupp. Edward produced evidence that the agent was not a virus: it was not deposited by high-speed centrifugalization, using centrifuges which deposit the smallest viruses; the agent cannot be transmitted from one animal to another, it does not multiply in tissue cultures, or produce inclusion bodies in the affected brains.

The question of the identity of the encephalitogenic agent from the glands of Hodgkin's disease with that obtained from normal bone-marrow has not been settled; this will probably be decided only when an antibody has been made from one, and tested against the other.

G. F. Madding, in reporting 6 cases of Hodgkin's disease of the stomach, concludes that clinically it is impossible to distinguish this rare condition from ulcer and from carcinoma of the stomach and that, although there are not any absolutely characteristic features radiologically, the presence of a diffuse lesion is suggestive. In 5 out of the 6 cases carcinoma was diagnosed before operation, and 3 of these patients were living 6 or more years after partial or complete resection of the stomach.

Differential diagnosis from histiocytic medullary reticulosis.—**Bodley Scott and Robb-Smith reported 4 cases, and collected 6 previously published cases which**

constituted a clinical and pathological entity for which the term histiocytic medullary reticulosis was suggested. These cases had been regarded as a form of atypical Hodgkin's disease, but the two conditions were quite different and not related in any way.

The clinical picture of histiocytic medullary reticulosis began with asthenia, emaciation, profound intoxication, and high, and sometimes relapsing, fever. The lymphatic glands were enlarged in 9 of the 10 cases; splenomegaly was present in all, the liver palpably enlarged in 8, and in the later stages jaundice occurred in 7. Anaemia was constant and more often normocytic than macrocytic; leucopenia was present in 7 cases, being so severe in 2 as to be associated with necrotic angina.

The course of the disease was rapid, from 6 to 32 weeks, the mean duration being 15 weeks. All the cases were in adults, and terminated fatally. Pathologically there was a systematized cellular proliferation throughout, and confined to the lymphoreticular tissues with siderosis most intense in the hepatic parenchyma and Kupffer's cells. The cellular proliferation and active phagocytosis were predominant in the medulla of the lymphatic glands; the proliferation in the medulla was composed of reticulum cells, large lymphocytes, and large pro-histiocytes, 12 to 14 μ in diameter with nuclei averaging 9 μ in diameter. In the spleen infarcts were frequent, but the lymphatic nodules (Malpighian bodies) were not prominent. The bone-marrow was commonly red, haemorrhagic, with firmer scattered white nodules

Baker, C., and Mann, W. N. (1939) *Guy's Hosp. Rep.*, **89**, 83
Desjardins, A. U. (1939) *Arch. Surg.*, **38**, 714
Edward, D. G. ff. (1938) *J. Path. Bact.*, **47**, 481
Harrell, G. T. (1939) *Arch. Path.*, **28**, 25.
King, D. P. (1938) *St. Thom. Hosp. Rep.*, 2nd ser. **3**, 68.
McNaught, J. B. (1938) *J. Amer. med. Ass.*, **111**, 1280.
Madding, G. F. (1938) *Proc. Mayo Clin.*, **13**, 618.
Robb-Smith, A. H. T. (1938) *J. Path. Bact.*, **47**, 457.
Scott, R. B., and Robb-Smith, A. H. T. (1939) *Lancet*, **2**, 194
Uhlenhuth, P., Wurm, K., Liebegott, G., and Gaupp, R., Jnr. (1939) *Z. ges. exp. Med.*, **105**, 205.
Wright, C. B. (1939) *J. Amer. med. Ass.*, **111**, 1286.

HYDATID DISEASE

See Surveys and Abstracts 1939, p. 376. **692-701**

HYDROTHERAPY

See Surveys and Abstracts 1939, p. 376 **703-707**

HYPERCHLORHYDRIA

See also Surveys and Abstracts 1939, p. 377 **Vol. VII**

DEFINITION

Erratum. In vol. VII, on page 2, second line from foot, for 'hydrogen concentration' read 'hydrogen ion concentration' **708**

The possibilities of investigating gastric secretion by stimulating the vagal gastric secretory centres in the brain by injections of insulin are discussed by Babkin, based on experiments on a dog. The chief advantage of using histamine or insulin for this purpose is that the gastric contents are not mixed with the substances administered, as they are in test meals given by mouth. Histamine, however, stimulates only the production of acid and, in some concentrations, inhibits the activity of the peptic cells. Insulin, on the other hand, by acting through the vagi, stimulates all the secretory elements in the gastric mucosa which are innervated by the vagi, and is therefore of use in studying the first, or vagal, phase of gastric secretion. After section of the vagi, or administration of atropine, insulin does not have this effect.

PHYSIOLOGY, PATHOLOGY, AND PATHOGENY

Hollander surveys the various possible factors which may play a part in maintaining the normal level of gastric acidity by lowering the concentration from approximately 0·6 per cent, at which it is poured into the gastric cavity from the parietal cells.

708 to the lower level normally found in test-meal examinations. (i) The test meal dilutes the secretion; the authors, however, have devised a method of correcting for this. (ii) Saliva has a diluting and a neutralizing effect, which can be reduced by getting the patient to expectorate his saliva during the investigation. (iii) Regurgitation of duodenal contents appears to be a minor factor. (iv) Variations in the composition of the parietal secretion are probably slight. (v) The possibility of reabsorption of hydrochloric acid by the gastric mucosa has not yet been adequately studied. (vi) There is strong evidence that the chief factor in lowering the gastric acidity is the production by the mucosa of one or more non-acid buffer-containing fluids, which also act by diluting the acid. The part played by pepsin in this direction is probably negligible, there is much more evidence for the existence of a specific non-acid diluting secretion which exerts an influence in the regulation of acidity; the arguments for and against the importance of mucus in this respect are at present contradictory.

The experiments of Wilhelmj on dogs, using Liebig's meat extract as a test meal have, as indicated in Vol. VII, p. 7, now been tried on humans by Upham and Spindler, who find that the meat-extract meal is the most satisfactory test meal yet devised, but that for its satisfactory performance laboratory assistance is necessary. The authors describe the curve illustrated by most so-called normal persons as having a sharp rise in acid secretion during the first half hour, followed by a fairly sharp fall; this is contrasted with the curves obtained from patients with duodenal ulcer with or without pyloric obstruction, in both of which the rise persists for an hour and reaches a higher level; they also describe the low plateau type of curve in cases of sub-acid gastric catarrh. Gall-bladder disease did not produce in their small series characteristic curves though the acid was generally below the normal level.

TREATMENT

Drugs

Nechelès, Neuweh, Steiner and Motel studied the toxicity and pharmacological action of the new antispasmodic drug diphenylacetyldiethylaminoethanolhydrochloride (trasentin). The drug was found to be 10 times more toxic to the dog than to the rat, 100 mg. per kg. body weight being the M.T.D. for the dog. In the human, single oral doses of 150 mg. and daily oral doses of 450 mg. continued for several weeks did not have any harmful effects. In its action this substance combined the properties of atropine and papaverine in that it abolished spasmodic contractions of smooth muscle produced either by direct stimulation or by indirect stimulation through the parasympathetic nerves.

Unhorn also conducted some clinical trials with trasentin on 24 gastro-intestinal cases (11 duodenal ulcers, 1 gastric ulcer, 1 duodenal diverticulum, 1 cardiospasm, 3 cholecystitis, 5 colitis, 1 hyperacidity, and 1 acute intestinal obstruction) giving the drug together with the usual other treatment, e.g. diet and alkalis. In cholecystitis and so-called cardiospasm, in both of which the pain is not caused by muscle spasm, no relief was obtained, but good results were obtained in the others. Patients with hiccough benefited particularly. Unhorn emphasizes the absence of toxic effects and of side-effects, such as dryness of the mouth, dilatation of the pupils, and circulatory disturbances.

Bennett and Gill investigated on a small series of hospital patients the claims made for colloidal aluminium hydroxide in the treatment of peptic ulcer (gastric, duodenal, and anastomosing). It has been claimed that aluminium hydroxide gel is preferable to alkalis for this purpose because, being amphoteric, it can neutralize hydrochloric acid without becoming basic, and that, in fact, it cannot produce an alkaline reaction. In 30 patients with peptic ulcer the gel was effective and did not produce alkalosis.

Babkin, B. P. (1939) *Amer. J. digest. Dis.*, **5**, 753.
Bennett, T. I., and Gill, A. M. (1939) *Lancet*, **1**, 500.
Unhorn, M. (1938) *Amer. J. digest. Dis.*, **5**, 121.
Hollander, F. (1938) *Amer. J. digest. Dis.*, **5**, 364.
Nechelès, H., Neuweh, F., Steiner, N., and Motel, W. G. (1939) *Amer. J. digest. Dis.*, **6**, 39.
Upham, R., and Spindler, F. (1939) *Amer. J. digest. Dis.*, **5**, 721.

HYPERIDROSIS

709 See Surveys and Abstracts 1939, p. 378.

HYPNOTISM

See Surveys and Abstracts 1939, p. 378. 711

HYPOGLYCAEMIA AND HYPERINSULINISM

See also Surveys and Abstracts 1939, pp. 72 and 378.

MORBID ANATOMY

Many more cases of tumours of the islet cells have been reported, especially in America and Germany; most were adenomas, but 2 or more were carcinomas 712

CLINICAL PICTURE AND COURSE

Chronic essential hypoglycaemia has become more prominent in the past 2 years Dorst described 2 types, one with a flat glucose tolerance curve and the other with a sharp rise followed by a drop to hypoglycaemic levels. The symptoms were asthenia, apathy, fatigue, and nervous irritability Graul reports cases of essential hypoglycaemia and hypotonia in groups of young men at puberty and women at the menopause.

Martin, Hellmuth, and Muth analyse the case-histories of 404 patients who had signs of hypoglycaemia but had not received insulin; in 341 the blood sugar fell below 70 mg. per 100 c.cm In 130 cases (32 per cent) there was an organic basis for the symptoms; in 219 (54 per cent) there was a non-organic functional basis; and in 55 (13 6 per cent) the basis was unknown In 286 cases there were no symptoms suggesting hypoglycaemia, in 82 cases there were symptoms suggesting hypoglycaemia, and in the remaining 36 there were definite symptoms of hypoglycaemia, namely weakness, nervousness, headache, trembling, lassitude, sweating, marked hunger, mental disturbances, and convulsive attacks Doubt is expressed about the correctness of ascribing psychoneurotic symptoms to hypoglycaemia, even if the blood sugar is low

Spontaneous hypoglycaemia has been described in a case of hypophysial hypoglycaemia with infantilism (Ricci); and hypoglycaemia of hepatic origin in an alcoholic woman (Minet, Warembourg, and Lunquette)

TREATMENT

Insulin Hypoglycaemia

Much work of great importance has been done on the insulin treatment of schizophrenia Day, Niver, and Greenberg report 28 observations, on 25 patients, in which the sugar in the blood and in the cerebrospinal fluid was estimated at frequent intervals Whereas the blood sugar dropped rapidly for 1 to 1½ hours, often to below 20 mg. per 100 c.cm , and then fell slowly to a level at which it remained more or less steady, the sugar in the cerebrospinal fluid was much more variable and erratic; in very few cases the sugar in the fluid, which at first was below the blood sugar, fell as low as the blood sugar. It is suggested by these workers that the sugar contents of the arterial and venous blood of the meninges more nearly approach each other and the sugar content of the cerebrospinal fluid than the arterial and venous blood in the arm

Dussik correlates the blood sugar and cerebrospinal fluid sugar in insulin hypoglycaemia with the symptoms and onset of coma In 18 cases the blood sugar reached its lowest point 2 to 3 hours after insulin and, although it remained below 30 mg. per 100 c.cm , coma did not supervene until about 4 hours after the insulin. When the sugar in the cerebrospinal fluid reached 50 to 40 mg per 100 c.cm or less, coma supervened although the blood sugar was rising. The curves intersected; the lowest cerebrospinal fluid reading was 22 mg. per 100 c cm. This, if confirmed, explains the findings of other writers (e g Heilbrunn) that coma does not supervene in schizophrenic patients till the blood sugar has remained at a low level for about 2 hours.

These observations throw light on the difficulty of correlating symptoms with the level of the blood sugar or degree of fall. If, as has been suggested (e.g Heilbrunn) the symptoms, especially coma, depend not on the absolute sugar content of the blood but also on the duration of hypoglycaemia, it may be that the sugar content of the cerebrospinal fluid is the determining factor. The sugar in the cerebrospinal fluid does not begin to fall till ½ to 1 hour after the blood sugar begins to fall (Day, Niver, and Greenberg).

712 De Morsier and Bersot described in detail the symptoms produced by an accidental hyperinsulinism in a morphine addict, which proved fatal in 3 days. The symptoms were classified as pyramidal symptoms: muscular twitching of face and limbs; tonic spasms of the face; spasms and tonic movements of extremities and trunk, complex iterative and rhythmic movements; epileptic crises; a large number of sensory symptoms; and vegetative and vasomotor symptoms. Boller also analysed the symptoms of hypoglycaemia, classifying them as vegetative, neurological, and psychotic.

Harris, Blalock, and Horwitz found that in the hyperinsulinism induced in psychotic patients, the amino-acids, potassium, and inorganic phosphates in the blood were decreased and the cholesterol and serum protein were increased. Keys, in similar observations, found that there is an increase in the serum proteins and sodium, and a fall in the non-protein nitrogen and potassium

The lowering of the potassium has been regarded as an important factor in determining the onset of coma Keys ascribed the changes in the potassium content to hyperactivity of the adrenals provoked by the hypoglycaemia.

Boller, R (1938) *Wien. klin. Wschr.*, **51**, 523.
Day, G. W., Niver, I. D., and Greenberg, M. M (1938) *Amer. J. clin. Path.*, **8**, 206
Dorst, S (1938) *Amer. J. med. Sci.*, **196**, 688
Dussik, K. T (1938) *Klin. Wschr.*, **17**, 769
Graul, G (1938) *Med. Klinik*, **34**, 961
Harris, M. M., Blalock, J. R., and Horwitz, W. A (1938) *Arch. Neurol. Psychiat., Chicago*, **40**, 116.
Heilbrunn, G. (1938) *Wien. klin. Wschr.*, **51**, 114
Keys, A (1938) *Amer. J. Physiol.*, **123**, 608
Martin, I., Hellmuth, G., and Muth, M. I (1937) *Amer. J. digest. Dis.*, **4**, 579
Minet, J., Waremboorg, H., and Linquette (1938) *Progr. méd., Paris*, 781
de Morsier, G., and Bersot, H. (1938) *Amer. J. Psychiat.*, **94**, Suppl., p. 143
Ricci, A (1938) *Gazz. Osp. Clin.*, **59**, 503

ICHTHYOSIS

713-719 See Surveys and Abstracts 1939, p. 379

IMMUNITY AND IMMUNIZATION

See also Surveys and Abstracts 1939, p. 379

ACTIVE IMMUNITY

721 In a review of his observations recorded during the last 12 years, Ramon discusses the effect on active immunization of various procedures which tend to decrease the toxic effects of immunizing injections, and increase the production of antibodies. The methods studied include the addition to the injected toxin or toxoid of substances such as tapioca, lanolin, and liquid paraffin, and the administration of repeated minute doses of toxin into the same area of subcutaneous tissue. The method of adding lanolin to the inoculum has also been applied to living bacteria such as *C. diphtheriae*, *B. anthracis*, and staphylococcus.

Analogous observations were made by Glenny on the use of alum-precipitated toxoid, and by Schmidt on toxoid precipitated by aluminium hydrate. According to Ramon, the lowering of toxicity and increase in immunizing potency induced by such procedures are due not to a direct action of the added material on the antigen concerned but to an effect exerted on the animal's tissues. This effect depends on an increase in the local inflammatory reaction with an associated delay in the rate of absorption. Of these two factors, the inflammatory reaction is probably the more important, since it has been shown that repeated subcutaneous injections of minute amounts of toxin produce a lessened toxic, but an increased immunizing, effect when the injections are given into the same site instead of into many different sites.

Another approach to the same problem, that of increasing the immunizing potency while diminishing the toxicity of antigens, especially bacterial antigens, may be

found in attempts to isolate from whole bacteria the different chemical fractions upon which their antigenicity depends. Most bacteria contain a multiplicity of such fractions, many of which are of little or no importance in the production of protective antibodies against the complete organism. In the case of some bacterial species, for example *Str. pneumoniae*, it has been possible to isolate in a fairly pure state those fractions upon which the production of protective antibodies in the immunized animal depends. Ekwurzel and his fellow-workers record field trials in the production of active immunity against pneumonia by single injections of purified pneumococcal polysaccharide. Topley and his colleagues isolated from *Bact. typhosum* a chemically pure and stable antigen having the immunizing properties of the whole bacterial cells. The result of field trials in the use of such a fraction for the production of typhoid immunity will be awaited with interest. 721

PRACTICAL APPLICATIONS OF IMMUNITY

Diphtheria

Refined antitoxin. - An important advance has been made recently in the concentration and purification of antitoxic sera. The method involves selective treatment with proteolytic enzymes by which the antitoxin-bearing molecules are modified; the molecules of 'refined' serum are approximately one-half the size of those present in the older type of antitoxic globulins, concentrated by precipitation with ammonium or sodium sulphate. Laboratory evidence suggests that the altered molecule of the antitoxin ensures more effective entry into the body cells (Glenny and Llewellyn-Jones). Additional advantages of the new serum are smaller volume for injection and a lower protein content, so that the incidence of serum sickness has been still further reduced. Clinicians may thus inject the serum with the expectation that undesirable reactions will not occur. 724

Alum-precipitated toxoid in human immunization. Improvements in preparation have increased the usefulness of this prophylactic (Chesney; Harries). Absorption and excretion are slow because of the relative insolubility of the aluminium-toxoid complex, so that the stimulation of the antibody-producing mechanism is greater after alum-precipitated toxoid (A.P.T.) than after toxoid-antitoxin floccules (T.A.F.), toxoid-antitoxin mixtures (T.A.M.), or formol-toxoid (F.T.). The use of T.A.M. and F.T. is decreasing in Great Britain, A.P.T. being now the prophylactic of choice for children under 8 years of age in whom undesirable reactions after injection are rare. In older children and in adults, A.P.T. sometimes causes local and even general symptoms, and is therefore less extensively used. T.A.F., the mildest of all prophylactics, being substituted T.A.F. should certainly be used when sensitiveness to prophylactics has been elicited by a 'detector dose' of A.P.T. in children, or a pseudo-positive Schick test in adults.

Numerous papers have been published confirming the observation by Glenny that 2 doses of A.P.T. at an interval of some weeks are much more effective than a single injection. All the published results in which an interval of 4 weeks is mentioned give a Schick-negative rate of at least 98 per cent. For inducing a high grade of immunity, the length of interval between the injections of any prophylactic is more important than the size of dose. When possible or convenient, the interval should be 4 weeks, but one of 2 to 3 weeks is preferable to the shorter period of one week formerly used. When 3 doses are given, the interval between second and third injections need not be longer than 2 weeks.

Schick test. Although the Schick test is undoubtedly of great value, it shares with other biological tests the defect of individual variation. It is becoming increasingly realized that there is not an exact level of antitoxin, but a Schick 'zone of immunity', which separates Schick-positive from Schick-negative individuals (Jensen, 1931; Parish and Wright). In general, it appears that 50 per cent of persons with $\frac{1}{10}$ to $\frac{1}{20}$ of a unit of antitoxin per c.cm. in their blood are Schick-negative, fewer persons with $\frac{1}{30}$, and only exceptional individuals with $\frac{1}{100}$ are negative. Similarly the zone extends in the other direction, but it is very rare to find a positive reactor with as much as $\frac{1}{5}$ unit.

Diphtheria in Schick-negative reactors. A number of cases of diphtheria, almost invariably mild, have been reported from time to time in Schick-negative reactors. The level of antitoxin corresponding to the negative reaction has been inadequate to ensure protection either because the infecting dose has been large or the strain of *C. diphtheriae* has been of unusually high virulence. For this reason many clinicians consider it advisable to inject one dose of diphtheria prophylactic into all 'natural' Schick-negative persons at the time of the Schick reading.

724 *'Relapse' from Schick-negative to Schick-positive.*—The titre of circulating antitoxin tends to wane in subjects who have few opportunities of contact with cases or carriers of toxigenic *C. diphtheriae*, e.g. in country districts and in certain institutions. The cells of the body, however, retain potential immunity throughout life, i.e. the power of rapid response to specific stimuli so that adequate antitoxin is produced when required. Diphtheria in individuals who have formerly been Schick-negative is relatively infrequent, and is usually mild. A number of cases are on record in which rapid recovery has taken place without treatment with antitoxic serum.

Re-inoculation of prophylactic.—To obtain a durable immunity to diphtheria, it may be necessary to give periodic re-injections of T.A.F. or A.P.T. (Parish and Wright). In some hospitals it is the practice to give members of the nursing staff one or more injections of T.A.F. every year. Children who have received 2 doses of A.P.T. in infancy may be given a third dose at the time of entry to school, and possibly a fourth dose at the age of 9 years. If children were re-inoculated as a routine in a community, the use of the Schick test might safely be curtailed.

Jensen (1937) suggested that nasal instillations of toxoid are a possible alternative method of maintaining circulating antitoxin at a level sufficiently high to ensure immunity. The method, which might prove very valuable, awaits confirmation.

Tetanus and Gas Gangrene

725 Following the production by Ramon of a potent immunizing anatoxin (formol-toxoid) from tetanus toxin, wholesale active immunization of the French army against tetanus has been adopted in conjunction with diphtheria and typhoid vaccination. Good results are claimed (Hardouin) and a similar system of immunization against tetanus is now employed on a voluntary basis in the British army (Boyd). From *welchii* toxin an alum-precipitated formol-toxoid has been prepared, this, it is claimed, is suitable for prophylactic vaccination against gas gangrene (Penfold and Tolhurst).

Ramon and his colleagues have described a method for the rapid induction of antitoxin immunity against tetanus or diphtheria. This consists in the simultaneous injection of antitoxin and toxoid, followed at suitable intervals by two further injections of toxoid. Experiments on rabbits indicate that the injection of a dose of antitoxin at the same time as the initial dose of toxoid exerts no inhibitory effect on the production of antitoxin by the animal's tissues in response to the stimulus provided by the toxoid.

Streptococcal Infections

727 Artificial immunization in the treatment of streptococcal infections has recently been partially eclipsed by chemotherapy. The mode of action of compounds of the sulphonamide group in combating infection remains obscure, but probably differs from that of immune bodies. For this reason there appears to be justification for the view that a combination of the two forms of treatment should prove more effective than either one used singly. The results of *in vitro* tests (Fleming), and of preliminary experiments in the treatment along these lines of artificially produced streptococcal infections in mice, appear to be in agreement with this hypothesis (Behrens), but await further confirmation. The same principle has been applied with apparent success in the treatment of human pneumococcal meningitis (Finland *et al.*) and in one case of typhoid fever (Harries, Swyer, and Thompson).

Enteric Fevers

728 *Vi-antigen.*—Serum prepared by the method recommended by Felix, and having a high content of Vi in addition to H and O antibodies, has now received therapeutic trial in the treatment of typhoid fever in 5 reported investigations (Felix, 1935; Robertson and Yu, McSweeney, Cookson and Lacey, Piper and Crocker.) In all 5 instances the serum has been found of value, but, apart from those cases reported by Felix, adequate controls have been lacking. There seems little doubt, however, that a favourable result has followed the administration of this serum in most cases, provided that doses were given sufficient to maintain a high concentration of Vi antibodies in the peripheral blood (Piper and Crocker). Methods for the titration and standardization of therapeutic antityphoid serum together with a suggested dosage of such a serum in the treatment of typhoid fever are discussed by Felix in a recent publication (1938, a). A further interesting development resulting from the discovery of the Vi-antigen has been the demonstration by Felix (1938, b) of Vi antibodies in the serum of a high proportion of chronic typhoid 'carriers' (see Part I, p. 50). Although the presence of these antibodies in the blood should not be

regarded as proof of the carrier state, Felix regards their demonstration as the best serological test available. 728

Behrens, E. (1938) *Zbl. Bakt., Abt. Orig.*, **141**, 385.
Boyd, J. S. K. (1938) *J. R. Army med. Cps*, **70**, 289.
Chesney, G. (1937) *Brit. med J.*, **1**, 807.
Cookson, H., and Facey, R. V. (1937) *Brit. med. J.*, **1**, 1009.
Ekwurzel, G. M., Simmons, J. S., Dublin, L. I., and Felton, I. D. (1938) *Publ. Hlth Rep., Wash*, **53**, 1877.
Felix, A. (1935) *Lancet*, **1**, 799.
— — (1938, a) *J. Hyg., Camb.*, **38**, 750.
— — (1938, b) *Lancet*, **2**, 738.
Finland, M., Brown, J. W., and Rauh, A. F. (1938) *New Engl. J. Med.*, **218**, 1033.
Fleming, A. (1938) *Lancet*, **2**, 74.
Glenny, A. T., and Llewellyn-Jones, M. (1938) *J. Path. Bact.*, **47**, 405.
Hardouin, A. (1937) *These de Paris*, No. 751, 55.
Harries, T. H. R. (1939) *Lancet*, **1**, 45.
Sawyer, R., and Thompson, N. (1939) *Lancet*, **1**, 1321.
Jensen, C. (1931) *C. R. Soc. Biol. Paris*, **108**, 539, 543, 552, 577, and 579.
(1937) *Proc. R. Soc. Med.*, **30**, 1117.
Loewenthal, H. (1939) *Lancet*, **1**, 197.
McSweeney, C. J. (1937) *Brit. med. J.*, **2**, 1118.
Parish, H. J., and Wright, J. (1935) *Lancet*, **1**, 600.
(1938) *Lancet*, **1**, 882.
Penfold, W. J., and Tolhurst, I. C. (1938) *Med. J. Aust.*, **1**, 604.
Piper, V., and Crocket, C. G. (1939) *S. Afr. med. J.*, **13**, 255.
Ramon, G. (1938) *Rev. d'Immunol., Paris*, **4**, 5.
Boem, A., Richou, R., Djourichitch, M., and Maccolini, R. (1938) *Rev. d'Immunol., Paris*, **4**, 24.
Robertson, R. C., and Yu, H. (1936) *Brit. med. J.*, **2**, 1138.
Topley, W. W. C., Raistrick, H., Wilson, J., Stacey, M., Challinor, S. W., and Clark, R. O. J. (1937) *Lancet*, **1**, 252.

IMPETIGO

See also Surveys and Abstracts 1939, p. 381.

CHRONIC IMPETIGO

Treatment

The sulphonamide group of drugs can be given to patients with confluent impetigo of the scalp and face of the type shown in Vol. VII, p. 95, this treatment is particularly suitable for adults but may also be used for children. The dose for adults is one 0·5 gram tablet 3 times daily for 10 days. Children and adults who have not responded well to prolonged local treatment have definitely improved with a sulphonamide compound but the drug must be given with great caution. 735

IMPOTENCE

TREATMENT

Organotherapy

The use of testosterone propionate in conditions with associated loss, or diminution, of sexual potency is described on page 57. 736

INDUSTRIAL ACCIDENTS

INCIDENCE AND COST

The following figures for the years 1936 and 1937 may be added to the table in Vol. VII, p. 119. 739

1936	7,606,066	2,286	459,271	461,557	661,592	5,786,345	6,447,937
1937	7,959,163	2,370	486,495	488,865	668,564	5,970,960	6,639,524

CAUSES

Extrinsic Factors

742 Vol. VII, p. 122, line 22: 'Factory and Workshop Act, 1901' should be altered to 'Factories Act, 1937'.

Vol. VII, p. 122, paragraph 5: the figures for 1938 are as follows. The chief Inspector of Factories reported (1938) that as a result of 308,061 visits paid to 549,972 factories and workshops in the year 1937, notices of contravention of regulations were served in 240,774 cases; 2,347 prosecutions were instituted against 853 firms; 336 of these charges were in respect of accidents entailing injury or death of workers.

TREATMENT

Availability of Treatment

744 There is a good deal to be said for the principle of bringing the system of Workmen's Compensation into closer administrative relation with that of National Health Insurance, and for providing that both be administered from a central department, payments being made to the disabled person through the Post Office, as in Germany. This would entail compulsory insurance against industrial risks, such as was introduced in the case of coal mining companies by the Workmen's Compensation Act, 1936 (the 'Nicholson Act'). The opinion has been widely expressed (e.g. by Wilson and Levy) that the State should regard the industrial worker as an important national asset, and that, when he becomes disabled by an accident, the State should take active steps to ensure that he is adequately treated, properly maintained during disability, and replaced in his former job, or trained and placed in a new job if necessary, as soon as he is fit to work again. At present he is left largely to his own devices in these matters, with the result that disability is often unnecessarily prolonged and the return to work made much more difficult than need be.

COMPENSATION FOR DISABILITY DUE TO INDUSTRIAL ACCIDENTS AND DISEASES

745 The present practice in France with regard to Workmen's Compensation is governed by the Law of 10th June, 1938, which came into effect on 1st January, 1939; this provides that payment of compensation shall begin on the first day following the accident (in most countries there is a 'waiting period', usually of 3 days, before such payments become due, this is intended to exclude minor accidents from the scope of the Acts). Half-wages are paid for the first month, after which, if disability persists, the rate is raised to two-thirds. Total permanent disability entitles the workman to three-quarters of his pre-accident wages, or to 100 per cent of these in cases in which the disability is so severe as to oblige him to employ someone to assist him in 'the ordinary acts of life', e.g. feeding and dressing himself; in such cases he can claim, in addition, any sum required to pay for such services, up to a maximum of 3,000 francs per annum. A claim which has been settled may be reopened at any time if disability recurs, or becomes aggravated by late complications. (In Great Britain this may be impossible unless a 'Declaration of Liability' has been filed.)

'Lump Sum' Settlements

It is the usual practice in industry to engage workmen by the week, and to pay weekly wages; following this convention, the industrial worker is accustomed to a weekly budget, so that payment of compensation is conveniently made in the same manner. In some cases, these payments may be commuted for a single payment, or 'lump sum', intended to redeem future liability. This is, for instance, provided for by Section 13 of the Workmen's Compensation Act, 1925, under which an employer is entitled to redeem his future liability in cases in which weekly payments have been made for not less than 6 months, the amount laid down as appropriate is such as would purchase an annuity from the National Debt Commissioners equal to 75 per cent of the weekly payments. This sum may be applied by the Court to the benefit of the injured workman.

It is, however, a common practice to negotiate a cash settlement once and for all of claims under the Acts even when disability has not lasted for 6 months, and for amounts which may be considerably less than the value of such an annuity. When liability under the Acts is disputed, the employer or his insurance company may propose a 'composition agreement', i.e. a settlement 'without prejudice'; he may

say, in effect, 'If I am liable to pay compensation at all, I should have to pay £100; it would cost me £50 to take the case to Court to test the question of liability; very well, I will pay you £50 to get rid of any liability in respect of this accident.' 745

Much hard bargaining takes place over such negotiations, in which the workman is often badly handicapped by lack of expert advice. An employer is not relieved of his liability by such an agreement unless it is registered in the County Court, but workmen do not always know this, and Courts are not always particularly careful to protect the interests of the workman. Wilson and Levy dealt exhaustively with the disadvantages of 'lump sum' payments, and these are severely criticized in the report of the International Labour Office on the Evaluation of Permanent Incapacity for Work in Social Insurance (1937). Sums so paid to the workman are often wasted, owing to his inexperience in handling a large sum of money. A careful investigation into the after-histories of 322 cases so 'settled' (which appears to be the only inquiry of this kind the results of which have been published up till now, 1939) was carried out by Norcross (1936), who concluded that this mode of dealing with workmen's claims 'fails in what it is trying to accomplish. The economic status of the claimants is not as good as under the bi-weekly system; their health conditions have not improved; their employment status is not strengthened; considerable sums of money are lost and larger sums unwisely spent, and injured workers and their families who ought to have compensation upon which to live become public charges.'

SUMMARY AND CONCLUSIONS

Wilson and Levy have published a careful study, with abundant references to authorities, dealing with many of the problems of industrial injuries, including an historical review of the workmen's compensation laws in Great Britain, and making valuable suggestions for improving these. 748

In 1936 an Interdepartmental Committee was appointed to report on the 'Rehabilitation of Persons Injured by Accidents', and this Committee issued an Interim Report in 1937 dealing with the treatment of fractures. Many cases of this type arise in industry, and form a substantial proportion of the more serious injuries.

In 1938 a Royal Commission was appointed in Great Britain with exceptionally wide terms of reference to inquire into the arrangements for treatment and compensation of workmen injured in industrial accidents, it is hoped that this body will make recommendations for great improvements on the present arrangements, and that due regard will be had to the experience of other countries, some of which are far ahead of Great Britain in the organization of this important branch of social service.

Ministry of Health. *Interim Report of the Interdepartmental Committee on the Rehabilitation of Persons injured by Accidents* (1937) London.

Norcross, C. (1936) *Vocational Rehabilitation and Workmen's Compensation*, New York.

Wilson, A., and Levy, H. (1939) *Workmen's Compensation*, Vol. 1, *Social and Political Development*, London

INFANT FEEDING

See also Surveys and Abstracts 1939, p. 381.

BREAST FEEDING

Quantity of Milk Secreted

Secretion of breast milk can be stimulated by the lactogenic hormone of the anterior pituitary; it can also be inhibited by any preparation of the follicular hormone, such as oestrone, which can be used with success when for any reason inhibition of lactation is necessary or desirable. 750

Relation of Maternal Diet to Lactation

Drugs of the sulphanilamide group administered to the mother during lactation are secreted in breast milk but not in sufficient quantity to be of any significance, or to affect the infant.

INFLUENZA

754 See also Surveys and Abstracts 1939, p. 383.

CLINICAL PICTURE

Complications

During the early months of 1939 a mild but wide-spread epidemic occurred. Post-influenzal cough, apparently due to tracheitis, was an outstanding feature, and sputum when present was usually heavily infected with pneumococci. Another interesting point is that many of the cases of otitis media resulting from influenza produced a pure growth of pneumococci from the pus. It is not unreasonable to assume that complications might therefore have been more severe were it not for the recent introduction of M & B 693 which was used widely, and probably with considerable help in view of the predominance of the pneumococcus as a secondary invader during the above period.

TREATMENT

Preventive

If a mask is worn during attendance on influenza patients it should protect the eyes, as infection can enter by this route.

INSOMNIA

755 See Surveys and Abstracts 1939, p. 386

INTELLIGENCE TESTS

TYPES OF INTELLIGENCE TEST

Individual Non-Verbal ('Performance') Tests

758 A Committee was set up in 1938 to prepare an English version of the 1937 Terman version of the Binet-Simon intelligence scale. It was expected that this would be available in 1939.

A non-verbal 'perceptual' test of intelligence, suitable for measuring intelligence in all subjects with a mental age above 3 years, has been prepared by Penrose and Raven, of the Research Department, Royal Eastern Counties' Institution, Colchester. These progressive matrices consist of 5 sets, each of 12 tests. A test is composed of a page of diagrams. The chief one is a rectangular figure covered by a geometrical pattern except in one area which is left blank. Below are 6 or 8 pieces the same shape and size as the blank area on the main diagram and covered with various patterns, the subject is asked to select the one which, when fitted into the blank area, would complete the pattern. A table of norms for subjects between the ages 6 and 14 is provided.

Davidson, M. (1937) *Brit. J. med. Psychol.* **17**, 93.
Miller, F. M., and Raven, J. C. (1939) *Brit. J. med. Psychol.*, **18**, 35.
Penrose, L. S., and Raven, J. C. (1936) *Brit. J. med. Psychol.*, **16**, 97.
Raven, J. C. (1939) *Brit. J. med. Psychol.*, **18**, 16.
and Waite, A. (1939) *Brit. J. med. Psychol.*, **18**, 40.

INTESTINAL OBSTRUCTION

See also Surveys and Abstracts 1939, p. 387

ACUTE INTESTINAL OBSTRUCTION

General Treatment

762 Wangensteen, Rea, Smith, and Schwyzer reported the results of treatment of all cases of acute mechanical intestinal obstruction of the small intestine seen at the University Hospital, Minneapolis, between June 1931 and June 1938; there were 156 patients and 190 cases, some being recurrences. There were 28 deaths in the series. In 66·3 per cent of all cases and 61·5 per cent of all patients (126 cases and

96 patients) duodenal suction was the primary treatment; among these there were 15 deaths, giving a patient mortality of 15·6 per cent and a case mortality of 11·9 per cent. Of 83 of these patients suction alone accomplished a satisfactory decompression in 64; there were 5 deaths in this series, giving a patient mortality of 7·8 per cent and a case mortality of 6 per cent. The authors confirmed the importance of this method in suitable cases, but emphasized the importance of differentiating (i) simple and strangulating types of obstruction, and (ii) acute obstruction in the large and small bowel. 762

Wangensteen, O. H., Rea, C. E., Smith, B. A., Jnr., and Schwyzer, H. C. (1939) *Surg. Gynec. Obstet.*, **68**, 851.

INTESTINES, TUBERCULOSIS

See Surveys and Abstracts 1939, p. 389. 776-778

JAUNDICE

See also Surveys and Abstracts 1939, p. 389.

TREATMENT OF JAUNDICE

Of Haemorrhage

From laboratory investigation and clinical trial at the Mayo Clinic, Butt, Snell, and Osterberg (1938) had success in the prevention and control of the haemorrhagic state of jaundiced patients in the pre-operative and post-operative periods by administration of concentrates of vitamin K, which is generally obtained from alfalfa meal, and animal bile-salts given in gelatin capsules by the mouth, injected intramuscularly, or, to control existing bleeding, by a duodenal tube administered slowly (30 to 60 minutes) by the drip method. Vitamin K acts by bringing back the prothrombin coagulation time to the normal. The prothrombin clotting time of jaundiced patients about to be operated upon should be taken and, if this is raised, concentrates of vitamin K with bile salts should be given until the prothrombin clotting time comes within normal limits. 788

Snell and his colleagues Clark, Dixon, and Butt have followed up their work at the Mayo Clinic on the use of vitamin K and bile salts in the treatment of the haemorrhagic diathesis in jaundice by new knowledge on the deficiency of prothrombin in various intestinal disorders in which the metabolism of prothrombin is so profoundly altered that spontaneous haemorrhage may occur, especially in intestinal obstruction, gastro-colic fistula, post-operative gastric retention, chronic ulcerative colitis, and intestinal fistulae.

The proper absorption and utilization of the fat-soluble antihaemorrhagic food factor (vitamin K), the alteration of which causes prothrombin abnormality, depend on the following circumstances. (i) The diet must contain the antihaemorrhagic factor, (ii) the bile must be normal; (iii) fat must be properly digested; (iv) a sufficient amount of normal intestinal mucosa must be available for absorption of vitamin K; and (v) the internal metabolism of prothrombin must be satisfactory, for which normal hepatic function is apparently essential.

In cases of post-operative intestinal obstruction in which trans-duodenal aspiration is continued for a considerable time, bleeding may take place from the anastomotic area, or from the intestine, this was previously ascribed to failure of the anastomosis or to leakage from blood vessels due to the underlying morbid process; but now it appears to depend on a fall of prothrombin due to lack of bile, thus preventing absorption of vitamin K. When haemorrhage occurs in intestinal obstruction it has been found that there is little bile in the intestinal tract. When alteration in the prothrombin content of the blood occurs in intestinal obstruction and other conditions, treatment by vitamin K should form part of the medical care. It is suggested that the concentration of prothrombin in the circulating blood should be estimated as a prelude to the treatment of bleeding in any medical or surgical cases in which there has been an inadequate intake or subnormal assimilation of food, diminution of the absorptive surface of the intestine, or prolonged diarrhoea. In some cases of intestinal disorder, and even in jaundice, it may be desirable to give vitamin K intramuscularly or intravenously, though intramuscular injection acts more slowly than the oral administration.

Butt, Snell, and Osterberg (1939) have continued their observations on the clinical

788 use of vitamin K, using a petroleum ether extract of alfalfa meal from which the pigments were removed by adsorption; 200 mg. of this extract was approximately equivalent to 66 grams of dry alfalfa meal and contained about 37,500 Dam units. The dosage in their patients has varied from 200 mg. to 8 grams of this crude concentrate daily, a total of 20 grams over 7 days has been given without ill effects. By the intramuscular route 13 grams in peanut oil, spread over 4 days, has been given.

To jaundiced patients whose prothrombin clotting time is normal, the authors give prophylactic treatment, 2 to 6 capsules each containing approximately 200 mg. of the concentrate, and 1 to 4 grams of animal bile salts, daily for 2 to 5 days before operation.

For jaundiced patients with a prothrombin clotting time raised to between 30 and 45 seconds the same treatment suffices. In those whose prothrombin clotting time is longer than 45 seconds they administer the vitamin together with bile salts by a duodenal or T tube employing the drip method: 2 to 4 grams of a water-soluble bile salt is dissolved in 250 to 500 c.cm. of warm physiological saline or tap water, and 1 to 2 grams of the alfalfa concentration is added. One such treatment generally brings the prothrombin clotting time back to normal.

For patients who have a raised prothrombin time, and who are actively bleeding, the clotting blood must be removed by lavage, the treatment described in the paragraph above is instituted, and a blood transfusion may help.

The authors have now treated with the alfalfa extract and bile salts 127 patients suffering from jaundice and submitted to some surgical procedure. In a large number bleeding was adequately controlled, but in some patients the treatment was ineffective. They emphasize the value of pre-operative treatment in preventing post-operative bleeding.

The authors have examined the prothrombin clotting time and the value of this therapy in other haemorrhagic states apart from that associated with jaundice, namely, menorrhagia, metrorrhagia, haemophilia, essential thrombocytopenic purpura, toxic purpura, essential haematuria, Banti's syndrome, uncomplicated haemolytic icterus, familial bleeding tendency, aplastic anaemia, and haemorrhagic duodenal ulcer, but found in every case that the prothrombin clotting time was normal, and that this treatment did not affect the tendency to bleed.

Stewart investigated the effect of administering vitamin K together with bile salts to 12 patients with obstructive jaundice and liver damage and one with post-operative external biliary fistula. He extracted the vitamin from fresh spinach, and mixed the extract with sodium taurocholate and sodium glycocholate in the proportion of 1 gram of extract to 4·5 grams of each of the bile salts. The dosage varied from 0·8 gram of the vitamin K-bile-salt preparation given on 1 day to 24·8 grams over 6 days, the average dose was 6·8 grams.

In all cases except one, obstruction to the flow of bile for over one week reduced the plasma prothrombin to less than 84 per cent., the average level was 53·4 per cent. Pre-operative treatment raised the plasma prothrombin level to an average of 86·2 per cent., in 2 cases to 100 per cent., and in one to 102 per cent.

Stewart found that the fall of plasma prothrombin after operation was only transitory, if feeding with the vitamin-K bile-salt preparation was resumed at once. He thinks that a prothrombin level of 75 per cent. is desirable before operation. He also found that, in the presence of hepatic damage, the prothrombin recovery was diminished.

Butt, H. R., Snell, A. M., and Osterberg, A. E. (1938) *Proc. Mayo Clin.*, **13**, 753
(1939) *J. Amer. med. Ass.*, **113**, 383
Clark, R. T., Jnr., Dixon, C. F., Butt, H. R., and Snell, A. M. (1939) *Proc. Mayo Clin.*, **14**, 407
Stewart, J. D. (1939) *Ann. Surg.*, **109**, 588

JOINTS, DISEASES AND DISORDERS

789-817 See Surveys and Abstracts 1939, p. 390

JOINTS, INJURIES AND INTERNAL DERANGEMENTS

818-825 See Surveys and Abstracts 1939, p. 392

KALA-AZAR

AETIOLOGY

826

Geographical distribution. - There is little real indication that kala-azar is spreading to new areas, but it is being recognized in a number of places from which it has not been hitherto reported. It has recently been shown to be wide-spread in South America. Isolated cases have been reported during the last 20 years, but on the whole these reports have been received with scepticism. The yellow-fever viscerotomy service in Brazil and the Argentine has been the agency through which light has been thrown on this subject: out of 47,000 viscerotomies, leishmania were found in 41 specimens. Subsequent clinical investigations in some of the infected areas brought to light a few cases of kala-azar. Nearly all the leishmania-infected viscerotomy specimens and most of the clinical cases came from the north-east corner of Brazil between Para and Bahia, but a few kala-azar patients were also found in the Chaco district of the Argentine. The cases were sporadic, and entirely unconnected with one another. Two species of *Phlebotomus* were found in this newly discovered endemic area. The causal organism is morphologically identical with *Leishmania donovani* and behaves like this organism in culture and in the gut of sand-flies, though it has received the name *L. chagasi*, there is little reason to doubt that it is a sub-variety of *L. donovani* (Chagas *et al.*).

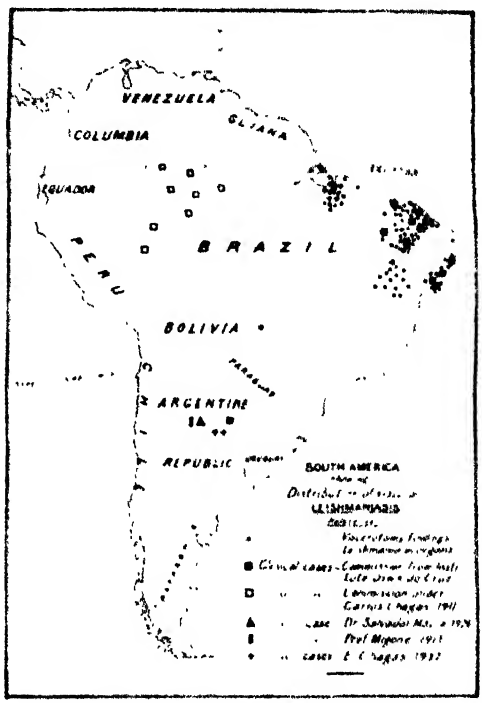


FIG. 3. Distribution of visceral leishmaniasis in South America

More adult cases have been found in the South of France recently, and a few cases from inland provinces. In the Adriatic an adult case has been reported from Venice, and in Yugoslavia the disease appears to be comparatively common. Here, as elsewhere, it is essentially a village disease. In one locality 7 per cent of dogs were found to be infected and *Phlebotomus major* was always present in the endemic areas. In Greece the disease seems occasionally to appear in epidemic form, and sometimes whole village populations have been infected.

An epidemiological study of the disease in the Sudan was recently carried out. It is confined mainly to the valley of the Blue Nile from the Abyssinian border to 150 miles south of Khartoum. This is open flat country with loamy soil, a high humidity, and a temperature which seldom falls below 60° F. The peak of the rainy season is August, and the kala-azar onset curve commences to rise in August, falling again in February (Henderson).

MORPHOLOGY AND LIFE-CYCLE OF *LEISHMANIA DONOVANI*

Transmission. - Little has been added to knowledge of the transmission of the disease. Recent epidemiological data appear to add weight to the hypothesis of

826 sand-fly transmission, and in all the new endemic areas some species of sand-fly has been found. In China, Sun and Wu found 11 naturally-infected sand-flies in a batch of 537 caught in an endemic area: they also showed that *P. chinensis* was a much more efficient carrier than other local species, in that this fly was most easily infected and that the infection survived a subsequent blood meal. Shortt and Swaminath have shown that the leishmania recovered from nasal secretions are viable.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Sternal puncture is a valuable method of diagnosis in kala-azar, and will undoubtedly largely take the place of splenic puncture. Many workers are now advocating this method, but Napier considered that, though a useful method, it was not as certain as splenic puncture.

The methods of serum diagnosis continue to multiply, but most are variations of Napier's original formalin method or Chopra's urea stibamine test and are based on the gross change in the albumin-globulin ratio that occurs in this disease. More delicate methods are favoured in Europe, but these are seldom applicable in tropical countries on account of the many cases of 'tropical splenomegaly' and other conditions that give confusing results. A method recently introduced is a photometric one using 1 in 1,000 serum and 1 in 100 urea stibamine solution (d'Oelsnitz).

TREATMENT

Kikuth and Schmidt have standardized the method of testing antimony preparations by treating infected hamsters, by this means solustibosan was selected for clinical trial. Weese reported that the tolerated dose of solustibosan was 25 per cent higher than that of neostibosan, and that it did not cause local irritation when injected. 80 per cent was excreted in the urine in the first 24 hours. Struthers and Lin, and Yates reported very favourably on its clinical use. Napier, who first used solustibosan clinically (see Vol. VII, p. 358, where it is referred to as Bayer 561) and reported good results, is not convinced that strict parallelism can be expected between therapeutic results in animals and in man; he considers that, gram for gram of antimony content, solustibosan is slightly but distinctly less efficacious than neostibosan, though it has certain other advantages which make it a very useful addition to the pharmacopoeia (Napier, 1937, and private communications).

A reactionary note was sounded by Laurinsich who still favoured tartar emetic. This opinion was based on extensive experience in a Naples paediatric clinic where 844 cases were seen in a period of 20 years.

Chagas, E., da Cunha, A. M., Castro, G. de O., Ferreira, I. C., and Romana, C. (1937) *Mem. Inst. Oswaldo Cruz*, **32**, 321.
d'Oelsnitz, M. (1938) *Mouvem. sanit.*, **15**, 220.
Henderson, J. H. (1937) *Trans. R. Soc. trop. Med. Hyg.*, **31**, 179.
Kikuth, W., and Schmidt, H. (1938) *Arch. Schiffs- u. Tropenhyg.*, **42**, 189.
Laurinsich, A. (1937) *Pediatria*, **45**, 857.
Napier, L. E. (1937) *Festschrift Bernhard Nocht zum 80. Geburtstag von seinen Freunden und Schülern*, Hamburg, p. 368.
(1939) *Lancet*, **1**, 959.
Shortt, H. E., and Swaminath, C. S. (1937) *Indian J. med. Res.*, **25**, 341.
Struthers, J. B., and Lin, J. C. (1937) *Chin. med. J.*, **52**, 335.
Sun, C. J., and Wu, C. C. (1937) *Chin. med. J.*, **52**, 665.
Weese, H. (1937) *Chin. med. J.*, **52**, 421.
Yates, J. M. (1937) *Chin. med. J.*, **52**, 339.

KIDNEY, SURGICAL DISEASES

See also Surveys and Abstracts 1939, p. 393.

MOVABLE KIDNEY

Diagnosis and Differential Diagnosis

832 Hess advised that pyelograms should be taken during full expiration and full inspiration on the same film ('respiration pyelography') to measure the amount of

mobility of the kidney. After operations for the fixation of the kidney they were of value in estimating the results. 832

HYDRONEPHROSIS

Treatment

Walters *et al.* summarized the results obtained in 46 out of a total of 71 plastic operations for non-calculous hydronephrosis performed at the Mayo Clinic. The types of operations and the numbers of each performed were: resection of renal pelvis, 36; resection of renal pelvis with re-implantation of ureter, 12; re-implantation of ureter 4; division and ligation of anomalous vessels, 3; ureterolysis, 3; uretero-pyelonephrostomy 5; and miscellaneous, 8. Of these patients 2 died, 8 were not followed up, and secondary nephrectomy was performed in 15 (21 per cent). Of the remaining 46, the final results were classified excellent, 5; good, 15; improved, 13; and not improved, 13. From this series no marked superiority or inferiority of any type of operation was noted. 833

CALCULI

Treatment

Priestley and Braasch followed up 177 patients with renal lithiasis who, for various reasons, were not submitted to operation. The late results were as follows: in 82 per cent of all unilateral cases and 98 per cent of all bilateral cases the stones caused further symptoms; 'silent' stones caused symptoms less often (67 per cent) than stones which had previously caused pain; other unfavourable factors were a large size, location in a calyx, especially in the tip of a calyx, presence of other abnormalities; impairment of renal function, and presence of infection. The authors conclude that surgical treatment is indicated for primary calculi unless they are so small that they may pass spontaneously. Oppenheimer emphasizes the importance of restricting operation in calculous disease to conservative measures whenever possible rather than nephrectomy. 834

TUMOURS

Primary malignant tumours of the kidney in infants and children have been reviewed by Campbell. He found records of only 2 cases of carcinoma in children; hypernephroma accounted for 2 to 11 per cent, but by far the commonest was the Wilms' tumour (embryomal adenomyosarcoma). Tumours of the renal fibrous capsule and of the renal pelvis were extremely rare. The mortality in cases of renal tumour treated by nephrectomy was about 95 per cent. Campbell considered that the only way to reduce this figure is by the use of intensive pre-operative and post-operative radiotherapy. 840

Cahill and Melicow investigated the significance of calcified deposits in renal tumours. Among 82 patients operated on, calcification, demonstrated by X-rays and by pathological study, was present in 12, in many cases it was secondary to haemorrhage and necrosis. The authors conclude that the presence of calcification renders the prognosis more grave.

Bailey and Harrison pointed out that large renal tumours are not always malignant. Of 68 renal tumours removed at the Peter Bent Brigham Hospital, Boston, there were 4 benign tumours weighing from 830 to 4,940 grams, a fifth patient had such a tumour but was not submitted to operation. The 4 who were operated on all did well and had no recurrence of the growth. In one case the tumour was a leiomyoma, and in the other 4 it was an adenoma.

Bailey, O. T., and Harrison, J. H. (1937) *J. Urol.*, **38**, 509.
Cahill, G. F., and Melicow, M. M. (1938) *J. Urol.*, **39**, 276.
Campbell, M. F. (1937) *J. Amer. med. Ass.*, **109**, 1606.
Cibert, J., and Klajman, H. (1937) *J. Urol. méd. chir.*, **44**, 273, 353.
Hess, E. (1938) *J. Amer. med. Ass.*, **110**, 1818.
Oppenheimer, G. D. (1937) *Surg. Gynec. Obstet.*, **65**, 829.
Priestley, J. T., and Braasch, W. F. (1937) *J. Amer. med. Ass.*, **109**, 1703.
Walters, W., Cabot, H., and Priestley, J. T. (1937) *J. Urol.*, **38**, 688.

LABOUR: II.—FAULTS IN THE FORCES

845-847 See Surveys and Abstracts 1939, p. 31.

LABOUR: III.—MALPOSITION AND MALPRESENTATION OF THE HEAD

OCCIPITO-POSTERIOR POSITIONS

Mechanism

849 For the first sentence in the last paragraph on page 453, read.
The occiput is usually primarily posterior, and one of three events may happen: (i) either it rotates backwards through an eighth of a circle and is born as a persistent occipito-posterior, or (ii) it rotates forwards through three-eighths of a circle and is born as an occipito-anterior position, the latter is the more usual; or (iii) occasionally the head is arrested in the transverse diameter during rotation from the posterior to the anterior position.

LABOUR: IX.—OBSTRUCTIONS IN THE SOFT PASSAGES

871 See Surveys and Abstracts 1939, p. 394

LABOUR: XI.—COMPLICATIONS OF THE THIRD STAGE

876-881 See Surveys and Abstracts 1939, p. 395

LABOUR: XII.—OPERATIVE AND MANIPULATIVE PROCEDURES

882-891 See Surveys and Abstracts 1939, p. 395

LABOUR: XIV.—ANAESTHESIA AND ANALGESIA

895, 896 See Surveys and Abstracts 1939, p. 396

LABOUR: XV.—RADIOLOGY

LABOUR

908 Caldwell *et al* have used X-rays to study the mechanism of labour in various types of pelvis, and consider that adequate radiological examination, together with greater experience in interpretation, will in the future enable a more accurate obstetrical prognosis to be made, although there are many factors affecting prognosis which cannot be measured by X-rays

Caldwell, W. E., Moloy, H. C., and Swenson, P. C. (1939) *Amer. J. Roentgenol.*, **41**, 305, 505, and 719.

LACRIMAL APPARATUS DISEASES

See also Surveys and Abstracts 1939, p. 397.

LACRIMAL OBSTRUCTION

Acquired

Treatment of Chronic Lacrimal Obstruction with Mucocele

913 A further development of Toti's operation has been described by Dupuy-Dutemps and by Grayer Morgan. The opening into the nose is made as large as possible and the mucous membrane of the nose is not removed but divided vertically and sutured to the sac wall.

Tumour

A tumour of the lacrimal sac resembling the mixed tumour of the lacrimal gland has been described by White, Michaelson, and Heggie. **913**

Dupuy-Dutemps, L., and Bourguet (1921) *Ann. Oculist., Paris*, **158**, 241.
— — — (1921) *Bull. Acad. Méd., Paris*, **86**, 293.
Morgan, O. G. (1938) *Trans. Ophthal. Soc. U.K.*, **58**, 163.
White, J. P., Michaelson, I. C., and Heggie, J. F. (1938) *Trans. Ophthal. Soc. U.K.*, **58**, 159.

LANDRY'S PARALYSIS

See Surveys and Abstracts 1939, p. 398 **917**

LARYNX DISEASES

See also Surveys and Abstracts 1939, pp. 90 and 398.

TUMOURS OF THE LARYNX

Innocent

New and Erich surveyed 722 cases of benign laryngeal tumours seen at the Mayo Clinic during 30 years; during this time 1,100 malignant tumours were observed. They divide the innocent tumours into 2 main groups: (*i*) true neoplasms or new growths, 329 or 45·6 per cent, and (*ii*) 'tumours' composed of any abnormal mass of tissue, 393 or 54·4 per cent. The first group comprised (*a*) tumours of epithelial origin (one adenoma and the rest papillomas), 195 or 27 per cent; (*b*) tumours of connective-tissue origin (myxomas), 58 or 8 per cent, angiomas, 26 or 3·6 per cent, and fibromas, neurofibromas, fibrolipomas, chondromas, and osterochondromas, all less than 1 per cent, (*c*) cysts, 35 or 4·8 per cent. In the second group, 332, or 46 per cent of the total, were inflammatory; the rest included xanthomas, amyloid tumours, epithelial hyperplasia and leucoplakia, and prolapse of the laryngeal ventricle. Tumours occurred on the vocal cords 10 times as often as in other parts of the larynx. The ages of incidence varied from 11 weeks to 76 years, but 35 to 50 years was the commonest age of onset: 70 per cent of the cases were male and 30 per cent female. The authors discussed these various types of tumour and gave special accounts of the histories of 37 cases. **926**

New, G. B., and Erich, J. B. (1938) *Arch. Otolaryng., Chicago*, **28**, 841.

LEAD POISONING

See also Surveys and Abstracts 1939, p. 400.

AETIOLOGY

Notification

For the paragraph on p. 658, Vol. VII, substitute the following:

The wide-spread use of lead in industry accounts for practically all the known cases of lead poisoning in Great Britain. The disease, if it occurs in a factory, is, by Section 66 of the Factories Act, 1937, compulsorily notifiable by medical practitioners to the Chief Inspector of Factories, Home Office, Whitehall, S.W.1; if affecting a person employed in the painting of buildings, the disease must similarly be notified under Section 3 of the Lead Paint (Protection against Poisoning) Act of 1926. **931**

Incidence

The following figures for 1938 may be added to the table showing the notified cases of lead poisoning (Vol. VII, p. 659) (the principal figures indicate cases and the raised figures deaths):

Notified Cases of Lead Poisoning

INDUSTRY	1938
Smelting of metals	2[1]
Plumbing and soldering	4[1]
Shipbreaking	13[1]
Printing	4[1]
Tinning of metals	—
Other contact with molten lead	5[1]
White and red lead works	9
Pottery	5[1]
Vitreous enamelling	—
Electric accumulator works	10[1]
Paint and colour works	8
Indiarubber works	—
Coach and car painting	1
Shipbuilding	5
Paint used in other industries	2[1]
Other industries	6
Painting of buildings (not notifiable until 1926)	22[1]
	96[1]

LEISHMANIASIS, CUTANEOUS

See also Surveys and Abstracts 1939, p. 401.

ORIENTAL SORE

AETIOLOGY

Epidemiology

933 An epidemic of oriental sore in the neighbourhood of Aleppo occurred when some refugees occupied a new partially cleared site on which they erected mud and straw-brick huts. Out of a total of 127 families, 45 were affected, 78 individuals having sores. The site abounded with sand-flies, when the clearing of the new site was complete, the number of sand-flies decreased and the incidence of oriental sore fell. A comparable though reversed state of affairs existed at Quetta after the earthquake, where the debris provided ideal conditions for the breeding of sand-flies, and oriental sore appeared in epidemic form. It was noticed that women who used cosmetics escaped sores on their faces, whereas in other women, in children, and in men the face was a common site.

Causal Organism

Hoare has drawn attention to a paper published in 1898 by a Russian writer, Borovsky, who described the parasite accurately and recognized it as a protozoon. This does not seem to vitiate the claim for priority made for Cunningham (1885) who described but, not unnaturally at this early date, was ignorant of the true nature of the bodies he saw and depicted from an oriental sore. It seems, however, that the name Borovsky should take the place of Wright (1903) who has hitherto been given the credit for first accurately describing and for recognizing the nature of the causal organism of oriental sore.

TREATMENT

Cure

Local

Holmes reported on the mass treatment of oriental sore amongst the troops who helped to clear the debris at Quetta. he, with most of his colleagues, preferred surgical measures with or without the intravenous injection of the trivalent antimony compounds, and reported poor results with the pentavalent compounds. The best results have been obtained when the sores have been scraped under an anaesthetic, treated with liquid phenol, and then elastoplast applied for 14 days without removal.

Hamburger pointed out that not all sores occurring on the North-West Frontier in India are due to leishmania; this may account for the disparity in the reports on the

result of treatment in oriental sore diagnosed clinically, which are still unfortunately the rule. Manson-Bahr recommended the following paint for oriental sores: 933

Cignolin	60 grains
Ichthammol	120 grains
Oil of cade	40 minims
Rectified benzene to	1 ounce

and for more chronic sores a similar ointment:

Cignolin	60 grains
Zinc oxide	240 grains
Olive oil	240 minims

SOUTH AMERICAN CUTANEOUS LEISHMANIASIS

AETIOLOGY

This disease appeared in epidemic form during the war in the Chaco district of Paraguay. Infection of the lymphatic glands occurred in 12 per cent of the cases. 934

Hamburger, H. J. (1939) *Indian med. Gaz.*, **74**, 151.
Hoare, C. A. (1938) *Trans. R. Soc. trop. Med. Hyg.*, **32**, 67.
Holmes, F. (1937) *J. R. Army med. Cps*, **69**, 258.
Manson-Bahr, P. (1937) *Festschrift Bernhard Nocht zum 80. Geburtstag von seinen Freunden und Schulern*, Hamburg, p. 278.

LEPROSY

See also Surveys and Abstracts 1939, p. 401.

PATHOLOGY AND BACTERIOLOGY

At the International Leprosy Congress in Cairo during March 1938, M. Soule confirmed his previous reports that he had cultured *Myco. lepræ in vitro* under certain conditions of gas pressure, and had carried the culture through more than 60 passages. 935

The first satisfactory infection of an experimental laboratory animal with leprosy was reported by Adler, who succeeded in inoculating Syrian hamsters with human leprosy. He reported (1937) that, of 4 animals inoculated, a heavy infection was established in 3 and a systemic infection, shown by the presence of lepra bacilli in liver smears, in the fourth. He splenectomized the animals and at the time of operation implanted in 3 of them a fragment of a human lepra nodule between the skin and the fascia of the abdominal muscles, distributing its fragments over a wide area in the neighbourhood of the incision. The animals also received an intraperitoneal injection of macerated leprous material. In the fourth case the nodule was embedded in the muscles of the left thigh. At the International Leprosy Congress in Cairo, March 1938, Adler demonstrated his results and reported that he had successfully inoculated another series of hamsters. Burnet confirmed these results by a positive result in one out of 6 hamsters inoculated, without preliminary splenectomy.

Adler, S. (1937) *Lancet*, **2**, 714.
Burnet, E. (1938) *Arch. Inst. Pasteur, Tunis*, **27**, 327.

LEUCORRHOEA AND OTHER NON-HAEMORRHAGIC VAGINAL SECRETIONS

See also Surveys and Abstracts 1939, p. 403.

LEUCORRHOEA

Vaginal Flora during Pregnancy

Woodruff and Hesseltine found that vaginal mycosis was present in 28 per cent of patients at the Chicago Lying-in Hospital during the last 3 months of pregnancy. 939

Treatment

Karnaky published a list giving the *p*H of various substances used for douches. Except when the discharge is due to monilia the following should be avoided:

939 sodium bicarbonate, sodium chloride, magnesium sulphate, iodine, potassium permanganate, and borax.

Roblee and Karnaky have independently shown that the addition of acid fermentable material to the vagina, and maintenance of the *p*H at 4 to 4·5, will cure most cases of cervical erosion.

Karnaky, K. J. (1938) *Radiolog. Rev.*, **60**, 172, 208
Roblee, M. A. (1938) *Amer. J. Obstet. Gynaec.*, **35**, 1039.
Woodruff, P. W., and Hesseltine, H. C. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 467

Vol. VIII LEUKAEMIA

See also Surveys and Abstracts 1939, p. 404.

MYELOCYTIC LEUKAEMIA

CHRONIC MYELOCYTIC LEUKAEMIA

Prognosis

941 In a recent study of 87 patients, the average duration of life after onset of symptoms was 4·2 years, 4 per cent of the patients survived for 10 or more years. Marked anaemia, relatively low leucocyte counts, and evidence of bleeding before beginning treatment indicate a short period of survival (Leavell).

CHRONIC SUBLEUKAEMIC MYELOSIS

947 A distinctive change in the radiographs in such cases is irregular density of the spongiosa of the long bones and throughout the flat bones, associated with decreased density of the corticalis of the long bones, the inner edge of the corticalis appearing frayed and irregular (Vaughan and Harrison). There may be increased red-cell thickness and fragility.

LYMPHOCYTIC LEUKAEMIA

CHRONIC LYMPHOCYTIC LEUKAEMIA

Prognosis

948 The duration of life is shorter in patients who have marked anaemia and high leucocyte counts when first seen (Leavell). The occurrence of skin lesions does not affect the prognosis.

MONOCYTIC LEUKAEMIA

950 The value of supravital studies in doubtful cases of monocytic leukaemia has recently been emphasized (Beck). The young monocyte in a case of leukaemia may, unlike the normal mature monocyte, show no motility. The frequency of skin lesions, especially exfoliative dermatitis, in chronic as well as in acute monocytic leukaemia, has been described (Montgomery and Watkins).

PUNCTURE OF THE STERNAL MARROW

MARROW CELLS, NORMAL AND IN DISEASE

955 *Subleukaemic leukaemia.* Scott considered puncture of the sternal marrow of particular value in subleukaemic lymphocytic leukaemia. The presence of more than 40 per cent of lymphocytes in the marrow suffices for a positive diagnosis. He doubted if a normal count excluded the condition.

Myelosclerosis. The differential diagnosis of myeloid leukaemia and myelosclerosis may present difficulties if the characteristic bone changes seen on radiological examination in the latter condition (Vaughan and Harrison) are not present. Sternal marrow puncture in such cases is of value. In myelosclerosis no definite cavity is present, and the marrow that is withdrawn, though cellular with many young forms present, does not show the predominance of one cell-type characteristic of the leukaemias (Scott).

Beck, R. C. (1938) *Amer. J. clin. Path.*, **8**, 509.
Leavell, B. S. (1938) *Amer. J. med. Sci.*, **196**, 329.

Montgomery, H., and Watkins, C. H. (1938) *Minn. Med.*, **21**, 636. 955
Scott, R. B. (1939) *Quart. J. Med.*, N.S. **8**, 127.
Vaughan, J. M., and Harrison, C. V. (1939) *J. Path. Bact.*, **48**, 339.

LICHEN

See also Surveys and Abstracts 1939, p. 405.

LICHEN PLANUS

Treatment

Recent investigations into the treatment of lichen planus of the tongue have shown the curative effects of thorium-X, which can be applied directly in the form of a varnish to the affected area. 957

LIPOIDOSES, THE

See Surveys and Abstracts 1939, p. 406. 963-966

LIVER DISEASES: I. LIVER FUNCTION TESTS

See Surveys and Abstracts 1939, p. 406 967

LIVER DISEASES: II. BLOOD VESSELS

PORTAL VEIN

Thrombosis

Treatment. Murray and MacKenzie investigated the effect of heparin, which had been shown experimentally and clinically by Murray and Best (1938) to prevent thrombosis in the systemic circulation, on portal thrombosis, its use in mesenteric thrombosis, and after splenectomy. Damage of the splenic vein was effected by the passage of a linen thread along its lumen for about an inch, and by severe crushing of this part of the vein. The spleen was then removed and the laparotomy wound closed. Ten days later the abdomen was again opened and the splenic vein was removed. 970

In 9 dogs thus treated the splenic vein was occluded by a thrombus in 7. Eight other animals were treated in a similar manner with the addition of continuous intravenous heparin through a catheter in the external jugulars after Jacobs' method. This injection was continued for 3 or more days so as to keep the clotting time of the blood about 20 minutes. Seven days after the injection of heparin the abdomen was again opened and the portion of the splenic vein previously damaged was examined. In all these animals the vein was patent, thus showing that heparin can prevent portal thrombosis after splenectomy.

Accordingly heparin was given intravenously to 8 patients after splenectomy; 6 of these patients were free from any untoward symptoms and are now quite well. In the fatal cases from generalized peritonitis the spleen was removed to facilitate gastrectomy for carcinoma of the stomach, and the portal system was free from thrombosis. Of 6 patients with mesenteric thrombosis, from whom portions of gangrenous intestine were removed, and who received heparin intravenously, 4 recovered; in the 2 fatal cases there was no further gangrene of the intestine, or extension of thrombosis; the results obtained in this, a condition estimated to prove fatal in from 85 to 95 per cent of cases, provide very striking evidence of the influence of heparin in the prevention of portal thrombosis, though the number of cases treated was small.

Jacobs, H. R. D. (1931) *J. Lab. clin. Med.*, **16**, 901
Murray, G., and MacKenzie, R. (1939) *Canad. med. Ass. J.*, **41**, 38.
Murray, G. D. W., and Best, C. H. (1938) *Ann. Surg.*, **108**, 163.

LIVER DISEASES: III.—CHRONIC VENOUS ENGORGEMENT

See Surveys and Abstracts 1939, p. 408. 971

LIVER DISEASES: V.—HEPATITIS, ACUTE AND SUBACUTE

973 See Surveys and Abstracts 1939, p. 408.

LIVER DISEASES: VI.– HEPATITIS, CHRONIC

See also Surveys and Abstracts 1939, p. 409.

AETIOLOGY

974 Bloomfield has investigated the aetiology of chronic hepatitis in 41 patients with the clinical picture of the disease. In 36 there was a history of alcoholism, but in the others the aetiology was obscure. Particular inquiry was made for a previous attack of acute hepatitis, and in 4 cases there was a history of jaundice, and he thought that in some cases after complete clinical recovery from an acute attack of hepatitis a latent hepatic insufficiency might persist and progress, leading to chronic cirrhosis. The initial stages of chronic hepatitis might be entirely latent, or latent with periodical exacerbations.

Connor (1938) claimed that the production of hepatic cirrhosis by alcoholism was now established, and considered that the first stage in this process was fatty infiltration, caused by the alcohol, the dietary insufficiency, and deficiency of vitamin B_1. He stated that prolonged fatty infiltration of the liver was an important mechanical factor in the production of fibrosis, and compared the similar sequence in diabetes mellitus, in which disease decreased oxidation of liver fat results in chronic fatty infiltration, which in turn may lead to hepatic cirrhosis indistinguishable from that caused by alcoholism. In alcoholic liver the stages of fatty liver, fatty liver with cirrhosis, and cirrhosis without fatty infiltration merge into each other and cannot be sharply divided. The final disappearance of fat in the late stages may be due to exhaustion of body fat, discontinuance of alcohol, and resumption of high-carbohydrate diet.

Connor (1939) has investigated the aetiology and pathogenesis of alcoholic hepatic cirrhosis, and emphasized the importance of inadequate diet, which is generally associated with the alcoholism. Food may be insufficient, or there may be insufficiency or absence of carbohydrate. This abnormal diet produces a fatty liver, which passes on in some cases to cirrhosis.

Bloomfield, A. L. (1938) *Amer. J. med. Sci.*, **195**, 429.
Connor, C. L. (1938) *Amer. J. Path.*, **14**, 347.
(1939) *J. Amer. med. Ass.*, **112**, 387.

LIVER DISEASES: VII. INFANTILE HEPATIC CIRRHOSIS

975 See Surveys and Abstracts 1939, p. 410.

LUNG DISEASES: I. ATELECTASIS AND COLLAPSE

AETIOLOGY

985 Among the aetiological factors of collapse, the relation between pulmonary collapse and infection of the accessory nasal sinuses has been pointed out by Paton Philip (personal communication) who demonstrated numerous cases of unilateral pulmonary collapse associated with infection of the maxillary antrum (sometimes with a fluid level) recognizable on X ray examination. In many of his cases there was re-expansion of the affected lung, with return of the displaced heart and trachea to the middle line after the sinus infection had been surgically treated.

CLINICAL PICTURE

Lee Lander recently called attention to the significance of localized emphysema as evidence of localized pulmonary collapse. Davidson referred to this in a discussion at the Royal Society of Medicine in which the early diagnosis of intrathoracic new growths was discussed. According to Lee Lander the diminution in size of a lobe due to obstructive collapse may cause localized compensatory emphysema, recognizable in a skiagram and perhaps the only detail which indicates the presence of localized pulmonary collapse. In such cases the well-known tri-

angular shadow may be absent, and displacement of heart or mediastinum may not be evident. Something has to fill up the space created by the shrinkage of the collapsed portion of lung, and this is effected by the compensatory emphysema. 985

Treatment

To the paragraph on acute massive collapse, Vol VIII, p 164, a cross-reference should be added to LUNG DISEASES: POST-OPERATIVE COMPLICATIONS, p 236, where a section is devoted to the prevention and treatment of this condition.

Davidson, M. (1939) *Proc. R. Soc. Med.*, **32**, 1342.

LUNG DISEASES: II.—OEDEMA

TREATMENT

Specific

The paroxysmal dyspnoea, often a precursor of pulmonary oedema, has been successfully treated by the administration of helium and oxygen mixtures. It is not certain that this treatment is specifically beneficial as the gas is always administered with positive pressure, which by itself often produces a satisfactory result. Helium is an inert gas with a molecular weight of 4, compared with a molecular weight of 28 for nitrogen. The lighter the gas, the greater is its rate of diffusion; if helium is substituted for the nitrogen of the air the resulting mixture will have an inherent mobility 3 times that of air, and therefore with such a mixture a greater amount of oxygen will reach the alveoli than if ordinary air is respired (Maytum). 986

The technique of administration using the Boothby-Lovelace-Bulbulian inhalation apparatus and a nasal or oro-nasal mask is described by Lovelace. He recommends that the mixture should never contain less than 20 per cent of oxygen.

Lovelace, W. R. (1938) *Proc. Mayo Clin.*, **13**, 790.
Maytum, C. K. (1938) *Proc. Mayo Clin.*, **13**, 788.

LUNG DISEASES: III. ABSCESS AND GANGRENE

See also Surveys and Abstracts 1939, p 410.

TREATMENT

Non-Operative

A comprehensive review of recent work on putrid lung abscess has been given by Barrett.

The use of short-wave therapy in purulent lung conditions has been discussed by Schliephake who reported on 45 patients thus treated, 3 suffering in addition from peritonitis, died, but the remaining 42 were completely cured. Brugsch and Pratt employed Schliephake's method but did not obtain favourable results in lung abscess and bronchiectasis.

Operative

There is a growing opinion among many thoracic surgeons in favour of early operation in cases of lung abscess. The most comprehensive reports on this subject are those by Neuhof and Touroff (1936 and 1938), who, in their earlier paper, reported the results of operation in 37 consecutive cases of acute putrid pulmonary abscess. They define the term 'acute' arbitrarily as indicating that the abscess is of less than 6 weeks' duration from the time of onset of the first symptoms definitely referable to it. 987

The second paper reported on 45 cases submitted to operation out of a series of more than 100 admitted to Mount Sinai Hospital, New York. The ages varied from 2 to 70 years. Of these 45 cases 34 were unperforated and 11 perforated. In unperforated cases bronchoscopy was of the greatest assistance in the accurate localization of the abscess. Operation consisted essentially in a single-stage procedure in which the lesion was entered through overlying pleural adhesions, unroofed, and packed.

The results were as follows: 2 deaths; recovery uneventful in 28 cases, and in the others accompanied by complications which were not serious. According to the authors' criterion of cure, 40 were cured, and in the other 3 the period of follow-up was too short to justify the word 'cure', but all were progressing satisfactorily when last seen. In addition to imperative indications for operation in this condition there

987 are a number of elective indications. The authors are adopting this method of treatment in an increasing proportion of cases.

Barrett, N. R. (1938) *St. Thom. Hosp. Rep.*, 2nd ser., **3**, 139.
Brugsch, H., and Pratt, J. H. (1939) *Amer. J. med. Sci.*, **197**, 653.
Neuhof, H., and Touroff, A. S. W. (1936) *Surg. Gynec. Obstet.*, **63**, 353.
— — (1938) *ibid.*, **66**, 836.
Schliephake, E. (1938) *Short-wave Therapy*, transl. by R. King Brown, 2nd ed., London.

LUNG DISEASES: IV. - TUBERCULOSIS

See also Surveys and Abstracts 1939, p. 411.

AETIOLOGY

988 Griffith, in discussing bovine tuberculosis in man, stated that 194 cases of bovine pulmonary tuberculosis had been reported in Great Britain; the highest incidence was in north-east Scotland and the lowest in the south of England. In one-third of these cases there was evidence that the alimentary tract was the portal of entry. Bacteriological evidence of transmission from a human case had been obtained, and evidence suggesting infection of cattle by a farm servant with infective sputum. Attention was directed to the danger of consuming raw milk, and reference was made to an investigation which reported that, of the 1¾ million children in elementary schools who drink milk regularly, at least 20 per cent receive raw milk from untested cows.

Epituberculosis

Burton Wood from a review of the history of 'epituberculosis' since the term was coined in 1920 concludes that, as the condition has now been more clearly defined, the term might be abandoned. Of the various explanations it appears that in most cases the chief cause is pulmonary deflation caused by bronchial occlusion by enlarged tuberculous bronchial glands. Scott-Pinchin and Morlock had previously come to the conclusion that epituberculosis was not a distinct entity but a manifestation of pressure exerted by enlarged glands at the root of the lung and thus causing bronchial obstruction and atelectasis.

MORBID ANATOMY

Hebert, in a lecture on fibrosis of the lungs, stated that in tuberculosis the fibrosis is essentially perifocal, though in some forms this is accompanied, followed, or masked by the interstitial type. The diagnosis of fibrosis from X-ray films is made far too often and indicates the diagnostic value of radiological findings. This is of importance in the diagnosis of fibrotic walls of cavities.

CLINICAL PICTURE

Senile Tuberculosis

Brooks and Lander collected 364 cases of pulmonary tuberculosis (309 men and 55 women) in which the first symptoms appeared between the ages of 50 and 82 years. The symptoms, in order of frequency of occurrence, were cough, cough with sputum, dyspnoea, loss of weight, haemoptysis, pleurisy, fever, gastro-intestinal symptoms, night-sweats, lassitude, and pleurisy with effusion. In 251 cases the sputum contained tubercle bacilli. The chief complication in this series was chronic bronchitis with emphysema (136 cases). Treatment in almost all cases was restricted to rest in bed. Statistical analysis showed that the mortality rate rose with increase in age of onset. The prognosis as regards duration of life improves as the number of years survived since the onset of symptoms increases. Nearly one third of the patients died within a year of the onset of symptoms.

TREATMENT

Curative

Operation.—Roberts, in a discussion of the part played by surgery in the treatment of pulmonary tuberculosis, urged the need for the provision of better facilities for such treatment in many parts of the country. Apart from the benefit to the patient,

collapse therapy causes early disappearance of tubercle bacilli from the sputum, even in many patients who subsequently die of the disease, and therefore is of great value in preventing spread of the disease. Freedlander and Wolpaw also reported on the benefit derived from thoracoplasty both in 'good chronics' and in 'slipping chronics', basing their conclusions on the comparison of the results of 85 operations with the fate of a control group of 58 patients who refused operation. 988

Important recent books on the subject are those of Hoyle and Vaizey, Alexander, and Sinding-Larsen, and the report by Bentley.

Alexander, J. (1937) *The Collapse Therapy of Pulmonary Tuberculosis*, Springfield, Ill.
Bentley, F. J. (1936) *Med. Res. Coun. Spec. Rep. Ser.*, No. 215.
Brooks, W. D. W., and Lander, F. P. L. (1937) *Brompton Hosp. Rep.*, **6**, 138.
Freedlander, S. O., and Wolpaw, S. F. (1937) *J. thorac. Surg.*, **6**, 477.
Griffith, A. S. (1938) *Proc. R. Soc. Med.*, **31**, 1208.
Hebert, G. T. (1939) *Tubercle, Lond.*, **20**, 145.
Hickling, R. A. (1938) *Quart. J. Med.*, **7**, 263.
Hoyle, C., and Vaizey, M. (1939) *Chronic Miliary Tuberculosis*, London
Roberts, J. E. H. (1938) *J. R. Inst. publ. Hlth.*, **1**, 857
Scott-Pinchin, A. J., and Morlock, H. V. (1933) *Lancet*, **1**, 1114
Sinding-Larsen, A. (1937) *National tryktheriet*, Oslo
Wood, W. B. (1939) *Tubercle, Lond.*, **20**, 205.

LUNG DISEASES: V.—SYPHILIS

MORBID ANATOMY

Bruce Pearson and de Navasquez reported 2 cases with one necropsy and summarized present knowledge of pulmonary syphilis. In secondary syphilis the infection generally spreads from the fauces and pharynx to the trachea and bronchi. In tertiary syphilis pulmonary involvement does not present any characteristic clinical or radiological picture, and diagnosis during life may be impossible. An uncomplicated pneumonic form is probably the earliest lung lesion, though at necropsy most cases show chronic interstitial fibrosis or gummata, which are later manifestations. Acute syphilitic pneumonia was present in one lung of one of the cases described. Pulmonary syphilis is always associated with, and secondary to, syphilitic aortitis and due to extension of infection from the mediastinum. This condition is not so rare as has hitherto been believed. 989

Pearson, R. S. B., and de Navasquez, S. (1938) *Guy's Hosp. Rep.*, **88**, 1

LUNG DISEASES: VIII. TUMOURS

See also Surveys and Abstracts 1939, p. 415.

MALIGNANT TUMOURS OF LUNGS AND BRONCHI

Primary

Morbid Anatomy

Tudor Edwards and Taylor record 4 cases of vascular endothelioma of the lung, of which they are unable to find any previous records; there was one man aged 26, and 3 women aged 48, 50, and 56. All 4 were treated by lobectomy, in one case 8½ years ago, and neither recurrence nor metastases have been observed. 993

Diagnosis

The method, introduced by Dudgeon and Wrigley, of examining fresh films of sputum for the presence of malignant cells is being increasingly used, and in a number of cases enables a diagnosis of malignant disease of the respiratory tract to be made when all other investigations have been indefinite. The method is as follows.

A fresh specimen of sputum is poured on to an unglazed porcelain tile. Film preparations, preferably of blood-streaked or solid portions, are made by spreading with a scalpel on a glass slide. The wet films are fixed in Schaudinn's fluid (one volume of absolute alcohol and 2 volumes of a saturated aqueous solution of mercuric chloride) to which is added immediately before use

993 glacial acetic acid to a strength of 3 per cent); the slide is immersed in the fixative for 20 minutes if possible, but 2 minutes will suffice. It is transferred to methylated spirit containing a few drops of solution of iodine and washed in distilled water. The film is stained in Mayer's haemalum for 2 minutes or less, and blued in tap water. Over-staining must be avoided. It is counterstained in eosin, dehydrated through the usual series of alcohols, cleared in xylol, and mounted in Canada balsam with a coverslip. About 6 films should be made from each specimen of sputum.

The results of sputum examination in 58 cases of suspected malignant disease of the respiratory tract are recorded. More recently Barrett has reported favourably on this method. Malignant cells have also been demonstrated in centrifuged pleural fluid.

TREATMENT

994 The considerable advance made in the surgical treatment of tumours of the lung has been reviewed by Brock. Radical lobectomy and total pneumonectomy with removal of associated lymph glands have now been performed in several cases and will undoubtedly be used increasingly. The largest series of such cases are those of Tudor Edwards, Reinhoff, and Overholt. Tudor Edwards (1938) advocated pneumonectomy in preference to lobectomy because of the extensive lymphatic intercommunications between the lobes.

Barrett, N. R. (1938) *J. thorac. Surg.*, **8**, 169.
Brock, R. C. (1938) *Lancet*, **2**, 1041, 1103.
Dudgeon, L. S., and Wrigley, C. H. (1935) *J. Laryng.*, **50**, 752.
Edwards, A. Tudor (1938) *Brit. J. Surg.*, **26**, 166
and Taylor, A. B. (1938) *Brit. J. Surg.*, **25**, 487.
Overholt, R. H. (1937) *Surg. Gynec. Obstet.*, **64**, 209.
Reinhoff, W. F. (1936) *Surg. Clin. N. Amer.*, **16**, 1459.

LUNG DISEASES: IX. POST-OPERATIVE COMPLICATIONS

995-1003 See Surveys and Abstracts 1939, p. 417.

LUPUS ERYTHEMATOSUS

TREATMENT

Chronic Discoid Type

General

1004 Barber reported benefit from treatment with prontosil of those cases in which it may be presumed that a chronic or latent streptococcal infection is responsible for the eruption. It is generally agreed that treatment with sulphanilamide gives satisfactory results in many cases of the chronic discoid type of the disease. The drug may be tried in acute disseminated lupus erythematosus. 2-sulphanilyl-aminopyridine commonly known as M & B 693, administered by mouth, has given satisfactory results in some chronic cases. Large doses of M & B 693 are usually not necessary, and the average dose is one tablet thrice daily. If a drug of the sulphonamide series is ordered, the patient must be instructed to omit eggs, onions, and cheese from his diet, and not to take 'health salts'.

Chajes recently drew attention to the beneficial effect obtained by injections of germanin (Bayer 205). Several of his cases described as cured, or improved, had been resistant to treatment with gold salts. Bayer 205 was injected intravenously in a 10 per cent solution, 5 or 7 days intervened between injections. The dose was from 0·25 to 1·0 g. Usually not more than 6 injections were given in any one series.

Barber, H. W. (1937) *Brit. med. J.*, **2**, 774.
(1938) *Lancet*, **2**, 670.
Chajes, B. (1938) *Lancet*, **2**, 1288.

LUPUS VULGARIS

See also Surveys and Abstracts 1939, p. 420.

TREATMENT

1005 *Light treatment.*- The use of the Finsen lamp in treatment is now being supplanted by the Finsen-Lomholt lamp technique. Aitken considers that, in the treatment of

lupus vulgaris, this lamp is superior to all others, and that it has shortened the duration of treatments and curtailed the length of time required to effect complete cure. 1005

Aitken, R. (1939) *Brit. J. phys. Med.*, N.S. 2, 193.

LYMPHATIC GLANDS DISEASES

See also Surveys and Abstracts 1939, p. 420.

CHRONIC AFFECTIONS

New Growths

Secondary

A. U. Desjardins stated that from the point of view of malignant metastases the retroperitoneal lymphatic glands, though perhaps not so often affected as the cervical glands, were the most important in the body. But, owing to their relative inaccessibility, little attention had been given to the relation between their involvement and the clinical picture produced. 1009

Anatomically the abdominal and pelvic lymphatic glands form a continuous system, but for purposes of description they may be divided into 2 main groups, (i) the iliac glands, and (ii) the abdomino-aortic glands which are subdivided into (*a*) the mesenteric, and (*b*) the para-aortic or juxta-aortic. Practically all the lymph from the abdominal and pelvic organs, as well as from the lower extremities, must pass through the para-aortic glands or through both the mesenteric and the para-aortic glands.

Many patients with carcinoma of the bladder, prostate, uterus, or rectum, or who have previously undergone partial or complete surgical removal of these organs seek medical advice because for some time they have experienced fresh symptoms—backache, abdominal pain, flatulence, and belching after meals, increasing size of the abdomen, and constipation. In addition to these symptoms of retroperitoneal metastases there may be increased deep resistance and tenderness on abdominal palpation in the epigastrium and in the umbilical, and sometimes in the hypochondriac regions. Lymph from the testes and ovaries normally drains directly into the upper para-aortic gland, and malignant tumours of the testis never give rise to secondary growths in the inguinal glands until the growth in the testis has perforated the capsule of the organ. The same is true of some primary tumours of the ovary. The same symptoms are caused by retroperitoneal metastases as those described in connexion with the bladder, prostate, and rectum. The clinical picture of retroperitoneal glandular involvement by Hodgkin's disease and lymphosarcoma differs somewhat from those given above (see under Hodgkin's disease, p. 101).

Desjardins, A. U. (1939) *Arch. Surg., Chicago*, **38**, 714.

LYMPHATIC VESSELS, DISEASES AND INJURIES

See Surveys and Abstracts 1939, p. 421 1010-1016

LYMPHOPATHIA VENEREUM

See Surveys and Abstracts 1939, pp. 155 and 421 1017

MALARIA

See also Surveys and Abstracts 1939, pp. 142 and 423

AETIOLOGY

Epidemiology

Strain of Parasite and Immunity

That immunity follows induced malaria in malaria therapy has been known since it was very clearly described by James. After induction of the disease by one kind of parasite, patients were often immune to further blood inoculation or the bites of infective mosquitoes with the same parasite, so that another species or strain had to be used if further satisfactory infection was required in treatment. 1018

Recent experimental work with bird and monkey malaria, and further observations on human malaria, have added greatly to the knowledge of such immunity.

Not only are there distinct species of parasite, e.g. in man, *Falciparum malariae, vivax, ovale*, and possibly *tenue*, but there appear to be many strains of these species, which are immunologically distinct though morphologically indistinguishable. Infections which protect against each other, i.e. are immunologically similar, are said to be homologous. Strains which do not mutually protect, i.e. which are immunologically dissimilar, are termed heterologous. Inoculation of an infected animal by an homologous strain gives rise to little or no effect, and this absence of effect is maintained for so long as the animal is infected, i.e. so long as parasites are present in the body even in greatly reduced numbers. In this condition, termed infection immunity or premunition, increased elaboration of the phagocytic macrophage mechanism is brought about after a time, so that parasites are maintained at a reduced level though liable at times to undergo an increase. This leads to a conception of infection in which periods, when infection is latent, are interrupted from time to time by periods when infection is active (relapses). There appear also to be humoral changes which favour or stimulate phagocytosis and so give rise to a kind of dual control shared between the humoral or phagocytosis-stimulating effect and the increase in the number of macrophages.

In addition to this type of immunity, the continuance of which depends on infection still being present and which specially characterizes many protozoal diseases, there is also evidence of some degree of a more lasting form of immunity independent of infection.

In human malaria the process of immunity is somewhat obscured by the number of different strains to which the subject is liable when living in a malarious locality. Repeated infections with one strain after another may in time lead to a sort of general immunity against prevalent strains, but this takes many years, e.g. the full period of childhood in many malarious communities, whereas Europeans living in the tropics rarely exhibit any approach to a strong immunity such as is so strikingly shown in experimental observations on laboratory animals.

PARASITOLOGY

Life Cycle

Considerable interest has been aroused by the discovery of a hitherto unsuspected 'X' cycle, or reticulo-endothelial cycle, of certain plasmodia of birds, in which cycle, since the parasite no longer utilizes the red cell as host, no pigment is produced, and the whole relation of the parasite to the infected organism is changed. Formerly the genus *Haemoproteus* ('Halteridium') was supposed to differ from the genus *Plasmodium* in that it possessed a multiplicative cycle in the endothelial cells, only the sexual forms appearing in the blood. Such a distinction, however, no longer holds good since *P. gallinaceum* and *P. cathemerium*, if not other seemingly typical bird plasmodia, have also an endothelial cycle. The pigmentless endothelial stage was at first thought to follow the sporozoite. In the two bird parasites mentioned, however, the 'X' cycle is not restricted to an initial multiplication, but may occur abundantly in later stages of the infection. The further suggestion has been made that such forms are responsible for relapses. Such a stage has been sought in human malaria, e.g. in material obtained by sternal puncture, but without any conclusive result. Most observers think that relapses in human malaria are not dependent on such a mechanism, and it is still unknown whether the 'X' cycle occurs in either monkey or human malaria.

Nomenclature and Description of Parasites

The subject of nomenclature is still of considerable complexity, but most of the issues have been recently made sufficiently clear in a paper by Christophers and Sinton.

Plasmodium ovale has now been recorded from Egypt and east Russia.

PATHOLOGY AND MORBID ANATOMY

Serological and Other Changes

Researches upon the nature of the flocculation reactions known as Henry's reaction continue. The diagnostic validity of these tests appears to be established. Trensz has summarized the position. During an attack the determination is of little importance compared with the search for parasites. But, in a patient who has recently been febrile and whose blood does not show parasites, negative results with Henry's reaction are of value as excluding malaria as a cause of that fever.

Serological curves are also of use in treatment. The curve continues to fall so long

as the drugs employed are exerting a favourable action. The technique must be standardized: it is a delicate reaction and variations in technique make it difficult to compare the results obtained by different authors. Samples of blood should be taken during non-febrile periods and when the patient is fasting, and should not be haemolysed.

Trensz advocated the use of solutions of melanin and the reading of results with a photometer. It appears probable that the reaction is not due to the presence of antibodies in the blood but to the serum constitution, namely the increase in euglobulins. Melano-flocculation is apparent 3 to 7 days after the attack, whereas antibodies take much longer to develop. The reaction is only produced in distilled water or hypotonic salt solutions, whereas antibodies act in isotonic or even faintly hypertonic solutions. Flocculation in distilled water runs parallel with melano-flocculation. The essential reaction is precipitation of the euglobulin, the melanin acting merely as an indicator, a function which can also be served by other substances, e.g. carmine.

TREATMENT

Prophylaxis

Communal

Antilarval measures.—Among methods recently employed directed to destruction of larvae may be noted those methods termed naturalistic, which aim at altering the biological environment in such a way as to be hostile to the larvae and so indirectly to reduce anopheline breeding. Of such methods may be mentioned the use of plants giving dense shade, much used in Assam where the breeding of *A. minimus* in the slowly flowing streams which form its natural habitat can be effectually controlled by such means.

Another method of this type found successful in Malaya is the covering of shallow water-courses with packed grass and herbage or with leaves of trees with twigs intertwined so as to form a brushwood drain. Of the more direct ways of destroying larvae, recently much employed, are 'sluicing' which, when it can be properly contrived, has been very effective in certain circumstances; various improved methods of applying Paris green (copper aceto-arsenite), which still remains the most effective and practical method of control by direct action, and the use of various types of waste products from oil refineries. The efficacy of this last type of oily larvicide is in the main dependent on the spreading properties of the substance on water, the readiness with which it wets and enters the tracheal system of the larva, and its additional toxic effect due to the more volatile constituents. All these factors, in addition to cost, must be considered when judging the respective usefulness of larvicides.

Measures against adult mosquitoes.—Of measures directed against the adult insects the spraying of huts has been strongly advocated, especially in some parts of tropical Africa. Methods of spraying have also been greatly developed as a means of preventing transport of infected mosquitoes by aeroplanes, the whole interior of the plane being sprayed by suitably arranged self-acting sprayers, using a non-inflammable insecticide.

Personal

Medicinal.—Methods of medicinal prophylaxis have received particular attention in the last few years. The recent report of the Malaria Commission of the League of Nations indicates the general principles involved and the dosage and method of administration desirable. The report also enables a comparison to be made between the efficacy of the new synthetic drugs and quinine as shown by a large series of experiments carried out in various countries at the League's suggestion. In medicinal prophylaxis a distinction must be drawn between drugs which can be used to prevent infection by destroying the sporozoites before these reach the trophozoite stage, i.e. so-called 'causal' or 'causative' prophylaxis, and those which act merely by controlling the appearance of active manifestations of infection in the form of clinical attacks of the disease. Although theoretically the former is an important objective, it is, with the drugs available, scarcely practicable, since the dosage necessary (e.g. with plasmoquine) is too near the possible toxic dose. Medicinal prophylaxis is therefore at present almost entirely a matter of controlling, rather than preventing, infection, and the usefulness of different drugs largely depends on their relative efficacy in this respect in moderate dosage and the degree of safety which attaches to their use in different circumstances. These considerations as given in the Malaria Commission's Report are very briefly summarized as follows:

Quinine.—A daily dose of 0·5 g. (7½ grains) of quinine hydrochloride sometimes causes temporary disappearance of *vivax* or *malariae*. A dose of 1·0 g. (15 grains) daily for 5 to 7 days is often necessary for the above purpose and to tide over a first relapse at some subsequent date. A dose of 1·3 to 2·0 g. (20 to 30 grains) is necessary in some countries for *falciparum* infection.

Atebrin.—A daily dose of 0·3 g. has a slightly more rapid action than quinine in 1·0 g. doses, and the absence of clinical symptoms is somewhat more prolonged. The effect with *falciparum* varies with the strain of the parasite. The treatment of relapses is more effective than with quinine. The spleen rate in treated indigenous communities decreases more slowly, but the effect is somewhat more lasting. It produces yellow discoloration of the skin.

Plasmoquine.—Used in small doses with quinine or atebrin, plasmoquine reinforces their action in the case of *vivax* and *falciparum*. It acts on the gametocytes of all three species. The small doses now used do not usually exceed 0·02 g.

In general therefore the effectiveness of quinine and atebrin is not greatly different, allowing for the larger dose of the former necessary. In favour of quinine is an almost complete freedom from risk of toxic effects, so that it can be used freely without medical supervision. Against quinine is the larger dose and the extremely bitter taste. Atebrin has serious disadvantages in the yellow coloration it causes if taken for any time and in its liability to cumulative effect. It is therefore still considered that its use should be under some degree of medical supervision.

The methods of using this drug in prophylaxis have been the subject of much investigation. The more usual use of the drug in tropical practice is a course of, say, 0·3 g. daily (given usually in 3 separate doses each of 0·1 g.) for 5 or at most 7 days (the usual treatment for an attack of fever) followed by a less frequent dosage, e.g. 0·3 g., 1, 2, or at most 4 days a week.

The actual practice by different observers, however, varies considerably. Thus Wallace, in the case of coolies, gave on 5 successive days 2 tablets at morning muster to each adult. In the afternoon one more tablet was given together with one tablet of plasmoquine simplex (0·01 g.). One tablet of plasmoquine simplex was then given alone on the sixth and seventh days and a follow-up treatment of 3 to 4 tablets on one or two days a week, in some cases continued for as long as four months. Rao and Cheluvarayan gave a mass treatment of 0·1 g. 3 times a day for 5 days in April and November (once every six months), a month after the second course 0·01 g. plasmoquine is given twice a day for five days and in addition during the fever season (ten months) a single dose of 0·2 g. of atebrin weekly. Sicault and Messerlin in French Morocco gave a standard treatment of 0·3 g. quinacrine (French atebrin) and 0·03 g. praequine (French plasmoquine) daily for 5 days followed by continuous treatment of one dose weekly. Others give merely the weekly dose. Ziemann gave for prophylactic purposes 0·05 g. of atebrin daily, or 0·2 g. twice weekly.

A case is recorded in which a half tablet of atebrin was taken daily for 2½ years. The skin appeared sunburnt but otherwise no effects were noted. According to Mezinesco and Cornelson yellow staining was present in 12 per cent of cases after 5 doses and in 82 per cent of 82 cases after 14 doses. In 6 per cent it lasted more than 5 months after cessation of prophylaxis.

The new drug certuna (chinonal) which, like plasmoquine, acts upon gametocytes but it is much less toxic, has been given in doses of up to 0·7 g. thrice daily for 7 days without toxic effects (Sioli). Missiroli and Mosna gave 0·12 g. a day for 6 days without any toxic effects. It appears to be at least as effective as plasmoquine as a gametocidal drug.

Cure

Antimalarial Drugs

With the exception of the drug certuna already referred to, no important new type of antimalarial synthetic compound has been put upon the market since the article on malaria was published. A considerable number of names, however, are encountered in the literature relating to drugs used in some countries either identical with, or very similar to, atebrin or plasmoquine (see below). Some new compounds of an entirely different type have also been shown to possess antimalarial properties, e.g. undecane diamidine and proseptasine, a sulphonamide compound, but at present these have no importance in the treatment of malaria.

Certuna (also referred to as chinonal) has the same general structure as plasmoquine. Its chemical composition was given by Kikuth and others as dialkylamino-oxyquinolylaminobutane. The name dialkylamino-butylamino-oxyquinoline is also

used, but neither name enables the formula to be given with certainty. The dosage is similar to that for plasmoquine.

The list below shows the many names that have been used for the same anti-malarial drug or for compounds believed to be identical, or nearly so. Some information on this point will be found in the Fourth General Report of the Malaria Commission (p. 480), and in the papers by Fourneau.

Atebrin (at first named erion): (i) quinacrine—French atebrin; probably identical with atebrin; first described as 866 R.P.; (ii) acriquine—Russian atebrin or closely related thereto.

Plasmoquine (at first termed beprochin): praequine French plasmoquine; probably identical with plasmoquine, plasmochin

Fourneau 710: (i) rhodoquine (French)—name rhodoquine now restricted to this compound (but see Fourneau 915, rhodoquine U); (ii) plasmocide (Russian) stated by Russian chemists to be Fourneau 710

Fourneau 915 rhodoquine U (French).

Primaline is similar to a combination of quinacrine and rhodoquine, i.e. it acts on both schizonts and gametocytes. Solvochin is quinine in weak alkaline solution. Paludex is a copper oxyquinoline preparation. Quinimax is the hydrochloride of quinine with some cinchonidine, other cinchona alkaloids, and resorcinol

Treatment of the Attack

Recent practice tends to a combined treatment rather than one in which a single drug alone is used, e.g. quinine treatment of the attack followed by atebrin after-treatment, or plasmoquine following quinine or atebrin treatment. The question of the most suitable treatment in all cases involves minimizing as far as possible the subsequent relapse rate. The following standard treatment for *vivax* infections in British troops in India was recommended by Amy and Boyd. The patient is put to bed and purged with calomel followed by Epsom salts. Quinine is then given until the initial febrile paroxysms are controlled. Quinine is then stopped and atebrin is given 0·3 g. daily for 7 days. The patient is then allowed to get up and receives 0·03 g. plasmoquine daily for a further 5 days. Admissions for malaria in British troops in India steadily declined from 18,878 in 1921 to 3,676 in 1934, this reduction is considered to be mainly due to reduction in the number of relapses, the decline in the relapse rate running *pari passu* with the introduction of plasmoquine.

Barrowman in Malaya gives all patients admitted to hospital 30 gr. of quinine a day for 2 days, then 4 tablets of atebrin a day for 4 days. The relapse rate following such treatment was only 9 per cent.

Intramuscular administration of atebrin (in the form of the musonate) is now commonly employed. Van Heukelom and Overbeek in a total of 875 cases gave to 634 cases 2 injections of 0·3 g. atebrin, followed by 0·3 g. by mouth daily for 3 days, starting 5 days after the last injection. The relapse rate was 4·4 as compared with 16·2 when atebrin injections alone were used.

Amy, A. C., and Boyd, J. S. K. (1936) *J. R. Army med. Corps*, **67**, 1, 83.
Barrowman, B. (1936) *Malay. med. J.*, **11**, 6.
Christophers, R., and Sinton, J. A. (1938) *Brit. med. J.*, **2**, 1130.
Fourneau, E. (1938) *Ann. Inst. Pasteur*, **61**, 799.
James, S. P. (1937) *Trans. R. Soc. trop. Med. Hyg.*, **31**, 263.
Kikuth, W. (1938) *Klin. Wschr.*, **17**, 524.
Mezinesco, M. D., and Cornelson, D. A. (1935) *Arch. roumain. Path. exp. Microbiol.*, **8**, 449.
Missiroli, A., and Mosna, E. (1938) *Riv. di parassitol.*, **2**, 55.
Rao, B. A., and Cheluvarayan, C. (1936) *Rec. Malaria Survey of India*, **6**, 447.
Sicault, G., and Messerlin, A. (1936) *Bull. Soc. Path. exot.*, **29**, 1023.
Sioli, F. (1938) *Klin. Wschr.*, **17**, 527.
The Treatment of Malaria (1937) Fourth General Report of the Malaria Commission of the League of Nations, *Bull. L. o. N. Hlth Org.*, **6**, 895.
Trensz, F. (1936) *Arch. Inst. Pasteur Algér.*, **14**, 353.
Van Heukelom, A., and Overbeek, J. G. (1938) *Geneesk. Tijdschr. Ned.-Ind.*, **78**, 1658.
Wallace, R. B. (1936) *Malay. med. J.*, **11**, 187.
Ziemann, H. (1937) *Arch. Schiffs- u. Tropenhyg.*, **41**, 73.

with the English form of statement. This Table is taken from the League of Nations' Annual Epidemiological Reports.

TABLE III. Puerperal Mortality (All Causes): Rate per 1,000 Live Births

Country	1925	1926	1927	1928	1929	1930	1931	1932	1933	1934	1935	1936
United States *	6·5	6·6	6·5	6·9	7·0	6·7	6·6	6·3	6·2	5·9	5·8	5·7
Australia	5·6	5·3	5·9	6·0	5·1	5·3	5·5	5·6	5·1	5·8	5·3	6·0
Canada †	5·6	5·7	5·5	5·6	5·7	5·8	5·0	5·0	5·0	5·3	4·9	5·6
Chile	6·1	5·8	5·8	5·9	7·8	6·8	7·5	7·1	8·4	9·1	8·5	8·5
Czechoslovakia	3·7	3·6	3·9	4·2	4·1	4·1	4·1	4·3	4·8	4·8	4·6	4·9
Denmark ‡	2·5	2·8	3·1	2·7	3·2	3·8	4·1	3·5	3·6	3·9	4·0	3·9
England and Wales	4·1	4·1	4·1	4·4	4·3	4·4	4·1	4·2	4·5	4·6	4·1	3·8
Estonia	3·8	4·1	4·1	5·0	4·6	4·9	4·2	3·4	3·4	3·4	.	3·6
France	2·4	2·5	2·9	2·9	3·0	2·7	2·5	2·6	2·5	2·5	.	.
Irish Free State	4·7	4·9	4·5	4·9	4·1	4·8	4·3	4·6	4·4	4·7	4·4	4·7
Italy	2·8	2·6	2·6	2·8	2·9	2·7	2·8	3·0	2·9	2·7	3·0	3·0
Netherlands	2·6	2·9	2·9	3·3	3·4	3·3	3·2	3·0	3·2	3·2	3·0	3·0
New Zealand	4·7	4·3	4·9	4·9	4·8	5·1	4·8	4·1	4·4	4·9	4·2	3·7
Northern Ireland	4·5	4·6	4·8	5·2	4·9	5·4	5·1	5·3	5·4	6·3	5·5	6·0
Norway	2·7	3·2	2·4	3·0	3·6	3·0	2·7	2·6	2·7	2·9	.	2·8
Scotland	6·2	6·4	6·4	7·0	6·9	6·9	5·9	6·3	5·9	6·2	6·3	5·6
Sweden	2·6	2·9	2·8	3·3	3·8	3·5	3·7	3·4	3·1	3·3	.	.

* Figures for the birth registration area (59·8 per cent. of total population in 1920, 94·7 per cent. in 1931, and 100 per cent. since 1933).
† Excluding the province of Quebec before 1926.
‡ Excluding the Faroe Islands.

CAUSES OF MATERNAL MORTALITY

Report of Departmental Committee on Maternal Mortality and Morbidity

Deaths Directly Due to Child-Bearing

The puerperal mortality rate includes deaths due to abortion, and the puerperal mortality-rates of England and Wales (based on total births) which during the years 1935, 1936, and 1937 were 3·94, 3·65, and 3·13 respectively, would have been reduced to 3·37, 3·16, and 2·78 respectively if the deaths due to abortion had been excluded.

The Inter-Departmental Committee on Abortion has now finished its deliberations and has presented its report (April, 1939) to the Secretary of State for Home Affairs and the Minister of Health.

PREVENTION OF MATERNAL MORTALITY

Specific Treatment for Puerperal Sepsis

Continuous work on this subject has been proceeding. The wonderful results obtained by the use of sulphanilamide and allied substances are recorded in the Report of the Medical Research Council for the year 1936-7 with the following cautions (p. 17):

"To the public it is necessary to give the warning that a powerful remedy must be used with care and discrimination and always under medical advice" and

"The method of chemotherapy exploits the margin between the lethal effect of a drug on the invading micro-organism and its toxic action on the patient. In some circumstances or with particular preparations of the drug, the margin may be narrower than usual: a few individuals, also, will always be found who are peculiarly sensitive."

While the paramount importance of Group A haemolytic streptococci in human infections has been confirmed, fatal infections in the puerperium by streptococci of Group B have recently been reported and some points of difference noted between these and infections by haemolytic streptococcus Group A (Fry).

Fry, R. M. (1938), *Lancet*, 1, 199.

MEASLES

See also Surveys and Abstracts 1939, pp. 77 and 424.

TREATMENT

Symptomatic

Specific Remedies

1027

Anderson conducted a critical examination of the value of sulphanilamide in the treatment of measles during the 1937-8 epidemic in Glasgow. Of 125 cases admitted to one hospital ward, 63 received sulphanilamide treatment and 62 did not; the treatment of the 2 series was otherwise exactly similar. The dosage was: under 5 years, 0·25 g. at 4-hourly intervals for 10 days, followed by 0·25 g. 3 times daily until dismissal; over 5 years, 0·5 g. at the same intervals for the same period. All cases in addition received 4,000 units of diphtheria antitoxin.

The sulphanilamide did not shorten the febrile period, its chief value lay in reducing the duration of broncho-pneumonia when this occurred as a complication, the average duration of broncho-pneumonia was 13·2 days in the control group and 8·3 days in the sulphanilamide group. Of other complications, those usually associated with streptococci occurred in 15 control cases and in 3 cases receiving the drug. The total incidence of complications in the control group was 47 complications in 30 cases, and in the sulphanilamide group 23 complications in 22 cases. Four deaths occurred, one in the control group and 3 in the sulphanilamide series.

Hogarth carried out a comparable investigation on 329 cases of measles during the 1937-8 epidemic in London, 159 patients were given proseptasine (*para*-benzylaminobenzenesulphonamide) during 10 days, and 170 served as controls. The dosage was: under 1 year, 0·5 g. 3 times a day for 5 days, and 0·5 g. twice daily for 5 days; 1 to 5 years, 1 g. 3 times daily for 5 days and 0·5 g. 3 times daily for 5 days; over 5 years, 1 g. 4 times daily for 5 days, and 0·5 g. 4 times daily for 5 days. He found that proseptasine reduced the incidence of complications due to haemolytic streptococci such as otitis media. The total incidence of complications was 26 (15·3 per cent.) in the controls, and 16 (10 per cent.) in the proseptasine series.

Anderson, J. (1939) *Brit. med. J.*, 1, 716.
Hogarth, J. C. (1939) *Brit. med. J.*, 1, 718.

MEDIASTINUM DISEASES

See Surveys and Abstracts 1939, p. 425.

1028

MEDICAL WITNESS

COURT PROCEDURE

Hearsay Evidence

1029

The Evidence Act of 1938, which came into force on the first of September 1938, extends the latitude already given in the Courts to the admission of secondary or hearsay evidence. It provides for the admission of documentary evidence as to facts which are in issue in a case, and any statement made by a person in a document which tends to establish such fact is now, on production of the original document, accepted by the Court as evidence of that fact, providing certain conditions are satisfied. These are:

1. The maker of the statement must have had personal knowledge of the matters dealt with; or
2. Where the document is one made by a person in the normal routine of keeping records in his professional capacity, or
3. If the maker of the statement is also called as a witness in the case, but where the witness would have been called had he been alive but is now dead or bodily or mentally unfit, a document made by him is admissible, provided it can be proved that he actually made it.

MEDICO-LEGAL EXAMINATIONS AND REPORTS

See also Surveys and Abstracts 1939, p. 426.

NOTIFICATION BY THE MEDICAL PRACTITIONER

Civil Cases

Industrial Disease

1030 Vol. VIII, p. 466, 7th line from bottom of page '1938' should read '1939'; and p. 467, line 16, '1938' should read '1939'. On p. 468 the following two additional scheduled industrial diseases should be added to the end of the list.

29. A localized new growth of the skin, papillomatous or keratotic, due to mineral oil, affecting a workman employed as minder or piecer in connexion with the process of cotton spinning by means of self-acting mules.
30. Poisoning by diethylene dioxide (dioxan) or its sequelae.

MEGACOLON AND ANAL ACHALASIA

See also Surveys and Abstracts 1939, p. 426.

TREATMENT

Operative

1031 In a discussion at the Proctological Section, Royal Society of Medicine, held during March 1939, interesting points raised were (i) the complete futility of operation on the sympathetic in megacolon in adults, although it was apparently useful in severe cases in boys, and (ii) the remarkable effect of spinal anaesthesia, which gave as great and as lasting results as sympathectomy, and should therefore take its place. Hurst considered that the occasional good results of sympathectomy might be due to the fact that spinal anaesthesia was used as a method of diagnosis by surgeons just before operation, and given sometimes for the operation, and that the actual operation might be without effect.

MENINGITIS

See also Surveys and Abstracts 1939, pp. 125 and 426.

TUBERCULOUS MENINGITIS

Aetiology

1037 Engel, Stern, and Newns have again emphasized the importance of the abdominal route of tuberculous infection in children, and the consequent importance of prophylaxis. In 3,214 necropsies at Great Ormond Street Hospital for Sick Children, there were 284, or 8·8 per cent, cases of tuberculous meningitis; in 41 of these (14·4 per cent) the primary infection was abdominal. Of these 41 cases, 28, or 67 per cent, occurred between the first and second years of life; there were 4 in the first year, 2 between 2 and 3, 4 between 3 and 4, and 3 between 4 and 5 years. In only 4 cases did the condition last longer than 2 months, and in only 3 of these were there obvious signs of peritonitis.

Engel, S., Stern, R. O., and Newns, G. H. (1938) *Brit. med. J.*, **2**, 1038

MENORRHAGIA AND METRORRHAGIA

1041-1043 See Surveys and Abstracts 1939, p. 430.

MENTAL DEFICIENCY

See also Surveys and Abstracts 1939, p. 431.

AETIOLOGY AND PATHOLOGY

Germ-Plasm Defect

1045 Penrose, dealing with the genetics of mental deficiency, showed that certain disorders in which amentia was prominent were definitely due to Mendelian char-

acters. Thus juvenile amaurotic family idiocy, phenylpyruvic amentia, familial microcephaly, and probably the Laurence-Moon-Biedl syndrome fitted in with the criteria pointing to a single rare recessive gene, whereas epiloia (tuberous sclerosis) was almost certainly a dominant character.

CLINICAL TYPES

Mongolism

Aetiology

Brain changes.—A. Meyer and T. B. Jones have carried to a further stage the histological investigations of the brain in mongolism, published by Meyer and Cook in 1937. In 10 cases of mongolism they describe remarkable brain changes, consisting for the most part of wide-spread proliferation of the fibrous glia. This overgrowth was largely in the pons and the medulla, and was either diffuse or circumscribed. It was of a distinctly perivascular nature and best seen with Holzer staining. The myelin and cell picture frequently showed no corresponding changes. No common factor was discovered which could account for the changes described. It is suggested that the incidence of pathological changes is greater in mongolism, owing to the peculiar constitution of the mongol, but that they are accidental rather than inherent. It is shown that the findings do not represent the pathological substrata underlying mongolism. 1047-1053

Phenylpyruvic amentia (phenylpyruvic oligophrenia)

This rare metabolic disorder was first described by Følling (1934), who reported 10 children in whom excretion of phenylpyruvic acid and mental defect were associated. Later Følling and Closs reported the presence of l-phenylalanine in the urine of 4 patients, and in the serum of 2. Jervis (1937) in America reported on 50 cases under his observation. The syndrome was characterized by the excretion of phenylpyruvic acid in the urine, pronounced intellectual defect, and neurological symptoms consisting of extrapyramidal manifestations and exaggeration of deep reflexes. Jervis considered that the condition is determined by a single recessive gene. Penrose also regarded the disease as due to a recessive gene.

Jervis suggested that the condition was caused by an inhibition in the metabolism of phenylalanine. In a subsequent paper (1938), describing experiments in which subjects of this disease were fed with various pure amino-acids and with phenylpyruvic and phenyllactic acids, he confirmed this view and concluded that these subjects were unable to oxidize the keto acid at a normal rate and therefore excreted it in excessive amounts in the urine.

Følling, A. (1934) *Hoppe-Seyl. Z.*, **227**, 169
and Closs, K. *ibid.*, **254**, 115
Jervis, G. A. (1937) *Arch. Neurol. Psychiat., Chicago*, **38**, 944.
(1938) *J. biol. Chem.*, **126**, 305
Meyer, A., and Jones, T. B. (1939) *J. ment. Sci.*, **85**, 206.
Penrose, L. S. (1938) *J. ment. Sci.*, **84**, 693

MENTAL DISEASES, HEREDITY

HEREDITARY MENTAL DISEASES

Schizophrenia and Manic-Depressive States

The hypothesis that the inheritance of schizophrenia depends on a single recessive gene is not altogether supported by recent reports. 1059

Elsässer examined 28 families in which both parents were psychotic. These families combined a total of 106 children, 47 per cent of whom were affected. In 10 cases both parents were schizophrenic; 50 per cent of their children were schizophrenic. In 6 cases one parent was schizophrenic and the other manic-depressive, 46 per cent of their children were mentally affected. Of the children of 2 pairs of manic-depressive parents, 65 per cent were affected. In 10 cases the parents suffered from an atypical psychosis and 47 per cent of their children were mentally affected. Half of the children who were not mentally affected were strange mentally. Of the grandchildren 10 per cent were psychotic and half the unaffected grandchildren were either schizoid or unstable. Among the 18 adult great-grandchildren 6 are strange but psychosis has not so far been observed in them. In one family in which the father

1059 was affected at the age of 17 by hebephrenic katatonia and the mother by stuporose katatonia, 5 of their 6 children are hebephrenic-katatonics and the other is schizoid.

Schulz examined 1,257 adult offspring in 386 families in which the parents were either psychotic or had close relatives mentally affected.

(A) In 141 cases both parents were mentally affected. These were divided into 2 groups. (i) The parents were either both schizophrenic, one schizophrenic and one manic-depressive, or both manic-depressive. In this group the probability of the children being psychotic was very great, particularly when both parents were schizophrenic. (ii) Among the parents in this group, either (*a*) one parent suffered from depression resulting from involution or senile or presenile melancholia, or (*b*) one parent suffered from induced mental disease and the other from schizophrenia or litigation mania. In this group there was less tendency for the offspring to be psychotic.

(B) In 84 cases one parent was mentally affected, the other parent was not affected but had a mentally affected brother or sister. The children in this group were less likely to be psychotic than those in group A.

(C) In 161 cases neither parent was mentally affected: one parent, however, had an affected brother or sister and the other parent had an affected parent, brother, sister, half-brother, or half-sister. In this group the proportion of affected children was less than in groups A and B.

The author concluded that these figures support the view that schizophrenia and manic-depressive psychoses are inherited as dominants.

Slater investigated the psychological constitution of the parents and children of 315 manic-depressives. The incidence of manic-depressive psychoses in the parents and children was 11·5 per cent. and 22·2 per cent. respectively. The incidence of schizophrenia 0·8 per cent. and 3·1 per cent. respectively. A survey of the literature shows that the incidence of manic-depressives is 0·38 per cent. As regards the type of inheritance, Slater thinks the evidence points to a sex linked factor.

Ziehen criticized the hypothesis of a recessive factor and put forward a complex hypothesis of a dominant specific factor coupled with a dominant inhibiting factor, schizophrenia developing only when the inhibiting factor is absent.

Galatschian has investigated the families of 214 schizophrenics, altogether 6,030 persons, and finds a rather higher incidence of schizophrenia in the blood relatives of schizophrenics than have previous authors. He tends to support the monohybrid recessive inheritance of schizophrenia.

Ebasser, G. (1939) *Z. ges. Neurol. Psychiat.*, **165**, 108.
Galatschian, A. (1937) *Schweiz. Arch. Neurol. Psychiat.*, **39**, 291.
Schulz, R. (1939) *Z. ges. Neurol. Psychiat.*, **165**, 97.
Slater, E. *Z.* (1938) *Z. ges. Neurol. Psychiat.*, **163**, 1.
Ziehen, V. (1937) *Arch. Psychiat. Nervenkr.*, **107**, 1.

METABOLISM, BASAL

1071-1076 See Surveys and Abstracts 1939, p. 432.

MIGRAINE

1077 See Surveys and Abstracts 1939, p. 433.

MOUTH DISEASES

See also Surveys and Abstracts 1939, p. 434.

FLOOR OF THE MOUTH

Mikulicz's Disease

1087 *Treatment.* It has been noted, particularly by Stanford Cade, that in some cases irradiation with X-rays, in a dosage of 2,000 *r* to each swelling, led to complete disappearance of the swelling.

JAWS

Tumours and Swellings

Tumours arising within the Bone

1090 Ewing's tumour also occurs within the bone of the lower jaw.

MUMPS

See Surveys and Abstracts 1939, p. 435. 1092

MUSCLE DISEASES

See also Surveys and Abstracts 1939, p. 436.

INJURIES

Treatment

1093 Treatment of minor muscle injuries by the injection of procaine hydrochloride (novocain) according to the technique of Leriche is increasing in favour. Leriche discovered that injection of a 'sprained ligament' with 10 or 20 c.cm. of 0·5 or 1 per cent procaine hydrochloride (novocain) resulted in permanent cure. Campbell gave several hundreds of injections for acute and chronic sprains of elbows, knees, shoulders, and fingers with satisfactory results in all cases but particularly in ankle and knee cases. In acute, not in chronic, sprains acute pain at the site of injection begins exactly 2 hours after the injection, lasts for 4 hours, and then as suddenly disappears, acute cases, therefore, should not be treated by this method, unless they are severe.

Smiley injected 20 c.cm. of a 1 per cent solution of novocain into the painful area in the calf in a case of 'ruptured plantaris tendon', the pain was greatly relieved, but the next day a small area of tenderness was still present and 30 c.cm. of the same solution was injected; this relieved the pain completely. Smiley considered that if at the first injection the area is injected so thoroughly that pain cannot be elicited by deep pressure or by the stresses it is designed to bear, a second injection should not be necessary.

Campbell, W. G. (1938) *J. R. nav. med. Serv.*, **24**, 48
Smiley, W. K. (1939) *Brit. med. J.*, **1**, 1138.

MYASTHENIA GRAVIS

See Surveys and Abstracts 1939, p. 439 1100

MYIASIS

See also Surveys and Abstracts 1939, p. 440

INFECTION OF NOSE, EAR, AND EYE

LARVA MIGRANS

1106 *Flies involved.* Probably, as was originally indicated, there are several causes of creeping eruption, and the form which is known in Natal and Zululand as 'sand-worm' eruption has been shown by N. I. Murray to be caused by a mite, some 300μ in length, which deposits its eggs in the burrows. It appears to be closely related to *Tetranychus molestissimus* which is found in the Argentine and Uruguay, where it attacks men and animals.

Murray, N. I. (1939) *Brit. med. J.*, **1**, 1026.

MYOPIA

See Surveys and Abstracts 1939, p. 129 1110

MYXOEDEMA

See Surveys and Abstracts 1939, p. 440 1111

NAILS, DISEASES OF

See Surveys and Abstracts 1939, p. 441 1112-1116

NARCOSIS, PROLONGED

See also Surveys and Abstracts 1939 p 442

RATIONALE

1118 Gerard has suggested that the results obtained from prolonged narcosis and from insulin, thyroid cardiazol and hyperpyrexial treatment are due to the increased oxidation of sugar in the brain which these methods of treatment all cause, directly or indirectly after interference with metabolism of the brain, as by hypoxaemia or hypoglycaemia a relatively long period of increased respiration and activity may follow it is also suggested that potassium ions which have leaked from the interior of the neuron during the period of hypoxaemia might provide the stimulus for this

Gerard R W (1938) *Arch Neurol Psychiat, Chicago* **40**, 985

NECK: TUMOURS AND OTHER MORBID CONDITIONS

1119-1124 See Surveys and Abstracts 1939 p 442

NEGLIGENCE, PROFESSIONAL

LIABILITY FOR NEGLIGENCE

Defences

1125 The Court of Appeal in the case of *Osborne v Mahon* decided that the doctrine of *res ipsa loquitur* could not be held to apply to a claim for damages for negligence when a swab was found to have been left in the abdomen The onus is still on the plaintiff to prove conclusively that the surgeon himself actually left the swab in the abdomen and that his action was negligent

Reference may also be made to the possibility of vicarious liability should the swab have been overlooked by the negligence of the nursing staff and this may be considered in relation to the two cases *Hall v Lees* (1904) 2 K B 602 and *Percovich v Freeman* (1866) 4 F and F 977

NEMATODE INFECTIONS, INTESTINAL

OXYURIASIS

1129 *Treatment* A diet of raw carrots an ancient and popular remedy for threadworms is extensively employed in zoological gardens to rid monkeys and other animals of this infection

Wright Bozicevitch and Gordon find that tetrachlorethylene when administered orally in a dosage of 0 1 c cm for each year of age and followed by a dose of magnesium citrate is effective The oral use of this salt may also be followed next morning by an enema containing 1 c cm of tetrachlorethylene in coconut oil soap solution

NEPHRITIS AND NEPHROSIS

See also Surveys and Abstracts 1939 p 443

CHEMICAL PATHOLOGY

1135 The second Congress on Renal Insufficiency at Evian was notable on account of a communication by Govaerts who affirmed that the importance of plasma protein drainage in the mechanism of oedema is no longer a matter of dispute, he gave a masterly review of the present state of knowledge of renal insufficiency with particular reference to the part played by the glomeruli and tubules respectively His study was largely based on the results of observations on urea and creatinine clearance

RELATION OF NEPHRITIS TO HYPERTENSION

1136 Experimental work on nephritis and hypertension continues, as a result of the pioneer observations of Goldblatt The most striking is perhaps that of Wilson and Byrom, who claim to have produced permanent hypertension in rats after partial

occlusion of a single renal artery. Morbid changes developed in both kidneys, and those in the unclamped kidney appeared identical with the lesions of 'malignant hypertension' in man. Nitrogen retention was not produced, but the animals were weak and wasted and had a tendency to convulsions and coma; the most striking observation of all was that excision of the partially occluded kidney was followed by complete recovery in the animals. **1136**

Rytand constricted the abdominal aorta in animals on the cardiac side of both renal arteries with resultant hypertension. When the kidneys had previously been excised hypertension was not produced. It is claimed that this observation demonstrates that the hypertension seen in cases of coarctation of the aorta is due to a pressor substance formed in the kidneys. Attempts to isolate definite pressor substances from kidneys remain inconclusive.

COURSE AND PROGNOSIS

Nephrosis

Murphy, Warfield, Grill, and Annis observed over a long period 9 patients with nephrosis; 2 died and no glomerular lesions were found at necropsy. They considered that the essential difference in prognosis justified the retention of the view that nephrosis was distinct from glomerulo-nephritis. **1138**

Glomerulo-Nephritis

Evidence of the usually benign character of acute glomerulo-nephritis was given by Murphy and Rastetter who noted that complete recovery occurred in 80 per cent of cases and that in a large number of them hypertension never appeared. At the same time they considered that some permanent damage occurred in all cases.

Govaerts, P. (1938) *L'Insuffisance rénale*, Paris, p. 57.
Murphy, F. D., and Rastetter, J. W. (1938) *J. Amer. med. Ass.*, **111**, 668.
Murphy, F. D., Warfield, L. M., Grill, J., and Annis, E. R. (1938) *Arch. intern. Med.*, **62**, 355.
Rytand, D. A. (1938) *J. clin. Invest.*, **17**, 391.
Wilson, C., and Byrom, F. B. (1939) *Lancet*, **1**, 136.

NEURALGIA, GLOSSOPHARYNGEAL AND TRIGEMINAL

See Surveys and Abstracts 1939, p. 445 **1145, 1146**

NEURITIS

See Surveys and Abstracts 1939, p. 446. **1147-1149**

NEUROFIBROMATOSIS

See Surveys and Abstracts 1939, p. 447 **1150**

NEUROSYPHILIS

See also Surveys and Abstracts 1939, pp. 154 and 447.

INTRACRANIAL SYPHILIS

GENERAL PARALYSIS OF THE INSANE

Treatment

Pyretotherapy. - In a report on fever therapy by physical means authorized by the Council on Physical Therapy of the American Medical Association, Krusen and Elkins report that fever produced by physical methods is as satisfactory as that produced by malaria in the treatment of general paralysis. The number of patients showing immediate clinical improvement is slightly greater with physically-induced fever, but some authorities anticipate a greater relapse rate. **1152**

SPINAL NEUROSYPHILIS

TABES DORSALIS

Diagnosis and differential diagnosis - Among the conditions from which tabes dorsalis must be differentiated is that of 'tonic pupils and absent tendon-jerks'. The **1158**

1158 diagnosis depends chiefly on: (i) the peculiar features of the tonic or 'pseudo-Argyll Robertson' pupil (see Vol. II, pp. 7 and 8), and (ii) the complete absence in the latter condition of the sensory features of tabes, namely pains and hypalgesia; (iii) the absence of ataxy and of Romberg's sign; and (iv) negative blood-Wassermann reaction and normal cerebrospinal fluid. The differentiation is most difficult in cases of mild tabes resulting in adult life from congenital syphilis, because in such cases the only abnormalities may be pupillary changes and absence of some tendon-jerks. The diagnosis then depends almost entirely on the state of the pupils.

Treatment

Pyretotherapy. In the report on fever therapy by the Council on Physical Therapy of the American Medical Association, mentioned above under General Paralysis of the Insane, it is stated that some observers consider that physically-induced fever is superior to malarial fever in the treatment of tabes dorsalis.

NEUROSYPHILIS DUE TO CONGENITAL SYPHILIS

1166 Congenital neurosyphilis is steadily and rapidly declining in frequency in association with congenital syphilis in general, but juvenile general paralysis of the insane and juvenile tabes dorsalis are not decreasing nearly as rapidly as the infantile manifestations.

Menninger made an exhaustive mathematical study of juvenile general paralysis of the insane and concluded that it occurred in about 1 per cent of all cases of congenital syphilis, and that its frequency was about one fiftieth of that of general paralysis of the insane from acquired infection. It affects males more often than females in the proportion of 4 : 3. The onset occurs on the average at the age of 13 years and, in 68 per cent of the cases, between the ages of 9 and 18. 60 per cent of the patients develop normally as regards their mentality until the onset of the disease, but the remaining 40 per cent are fundamentally retarded in their mental development.

According to Purdon Martin's observations, and analysis of the records of the National Hospital, cases of juvenile tabes fall into two groups. (i) Severe cases, with positive Wassermann reaction: the onset is usually about puberty but may be much earlier, optic atrophy is the outstanding symptom and is associated most commonly with fixed or Argyll Robertson pupils and absence of tendon-reflexes. Mild ataxy and superficial sensory disturbances develop in the course of years and a considerable proportion of the patients become mentally affected, and pass into a state of tabo-paresis. (ii) The larger group comprises mild cases which are almost always completely Wassermann-negative. The patients have, as a rule, reached adult life before any abnormality is observed and in many instances come under observation because of some symptom which is not tabetic. Abnormal pupils and lack of tendon-jerks are then observed. Most of these cases are very slowly progressive and some remain stationary. Optic atrophy may rarely ensue, and fits sometimes occur in these patients. In spite of the negative serological tests, antisyphilitic treatment should be given if there is any sign of activity of the disease.

Krusen, F. H., and Elkins, I. C. (1939) *J. Amer. med. Ass.*, **112**, 1689.
Menninger, W. C. (1934) *Amer. J. Syph.*, **18**, 486.
(1935) *J. nerv. ment. Dis.*, **81**, 489.

NOSE AND NASOPHARYNX DISEASES

See also Surveys and Abstracts 1939, pp. 90 and 449.

NASOPHARYNGEAL TUMOURS: LYMPHO-EPITHELIOMA

1168 Cappell and Capps both reported series of cases of lympho-epithelioma of the nasopharynx. Cappell regarded this as a distinct type of tumour, arising generally in the lymphoid tissue of the nasopharynx and tonsils and less often in the hypopharynx; he discussed an earlier series of 12 cases, 3 other's reported, and 6 new cases, making a total of 21. The origin of these tumours was not certain; they have occurred at all ages, in young children and in one case at 82 years of age. The commonest site is close to the mouth of the Eustachian tube, in which position unilateral deafness may be the first symptom. Later symptoms are difficulty in opening the mouth (due to invasion of the internal pterygoid), nasal obstruction,

difficulty in swallowing and in speaking, and cranial nerve palsies (due to invasion of the base of the skull at the foramina for the cranial nerves). Bilateral enlargement of cervical lymph nodes takes place early. Later there is wide-spread metastasis, especially in the spine and liver. These tumours are especially radio-sensitive; surgery, except for biopsy, is contra-indicated. Four of Cappell's patients have survived for 5 years after irradiation therapy, 3 treated with radium and one with deep X-rays. Capps recommended starting treatment with tele-radiation. If this fails he advised supplementing the dose with applied or interstitial radium or radon seeds. The prognosis is grave unless treatment is started early. **1168**

Cappell, D. F. (1938) *J. Laryng.*, **53**, 558.
Capps, F. C. W. (1939) *J. Laryng.*, **54**, 133

NYSTAGMUS

AETIOLOGY AND PATHOLOGY

Nystagmus may be due to toxic causes and in particular to barbiturate intoxication. In some cases of prolonged alcoholic excess the patients become unable to fix steadily and show with all positions of the eyes a very irregular nystagmus of rather large amplitude which gives them a 'shifty' expression. **1169**

NYSTAGMUS OF THE PALATE

Guillain summarized the knowledge gained at the Salpêtrière on the syndrome of synchronous rhythmic palato-pharyngo-laryngo-oculo-diaphragmatic myoclonus, generally known as nystagmus of the soft palate. Myoclonus of the muscles of the neck, trunk, and limbs has been associated. When the eyeballs are affected the myoclonic movements are oscillatory and differ from those of true nystagmus. The rhythm of the contractions is always the same in the same patient and in the various organs affected, but varies among individuals from 80 to 180 per minute. The author stated that neither scopolamine, stramonium, physostigmine, morphine, nor ergotamine tartrate had any effect on the myoclonus, but that it might sometimes be inhibited voluntarily or on the advent of paralysis in the region involved. He stated that, in three-quarters of the cases, the causal lesions were vascular, and that the condition had sometimes followed epidemic encephalitis. He concluded that olivary lesions were present in all cases adequately examined, and considered that the olivo-dentate system was of great importance in this condition. When unilateral, myoclonus is homolateral with regard to the dentate nucleus and contralateral with regard to the olive. **1173**

Guillain, G. (1938) *Proc. R. Soc. Med.*, **31**, 1031

OEDEMA

See Surveys and Abstracts 1939, p. 450 **1174**

OEDEMA, HEREDITARY

See Surveys and Abstracts 1939, p. 450 **1175**

OESOPHAGUS DISEASES

See Surveys and Abstracts 1939, p. 450 **1176-1188**

OVARY DISEASES

See Surveys and Abstracts 1939, p. 451 **1191-1196**

OXYCEPHALY

See also Surveys and Abstracts 1939, p. 453

AETIOLOGY

Burkens, La Chapelle, and Groen published the pedigrees of 2 cases of oxycephaly, from which it was concluded that the disease is due to a mutation transmitted as a **1198**

KEY NUMBERS

1198 sex-linked dominant. They rejected the hypotheses of Marie-Sainton (that the condition was a disturbance of ossification of membrane), and of Jansen (of intra-uterine disturbance due to the pressure of a tight amniotic band), and regarded the condition as a disorder of the genes.

Schwarzweller considered that the condition was a hereditary malformation for the following reasons: (i) the existence of transmitted cases; (ii) the appearance of certain isolated symptoms in other members of the family; and (iii) the frequent association of this and other malformations due to arrested development. He suggested that affected females should be sterilized.

Burkens, J. C. J., La Chapelle, E. H. and Groen, J. (1936) *Ned. Tijdschr. Geneesk.*, **80**, 5547.
Schwarzweller, F. (1937) *Z. KonstLehre*, **20**, 341.

OZAENA

1199 See Surveys and Abstracts 1939, pp. 90 and 453.

PAIN

1200 See Surveys and Abstracts 1939, p. 454.

PALATE, CLEFT, AND HARE-LIP

1201, 1202 See Surveys and Abstracts 1939, p. 454.

PANCREAS DISEASES

1203-1208 See Surveys and Abstracts 1939, p. 455.

PAPILLOEDEMA

1209 See Surveys and Abstracts 1939, p. 458.

PARAGONIMIASIS

PARASITOLOGY

1210 Chen reported that in Canton the rat (*Mus norvegicus*) had been found to be a natural host of *Paragonimus*.

Diagnosis

Wang and Hsieh believed that X-ray examination of the lung was of diagnostic value.

Treatment

To and Ko stated that they had treated successfully 2 fresh cases of paragonimiasis, and with improvement 2 others previously treated with emetine hydrochloride, by subcutaneous injection of 5 per cent carpain hydrochloride in physiological saline. The total quantities injected were, 0·3 g. in 6 days; 1·1 g. in 23 days; 0·5 g. spread over 10 days; and 0·9 g. in 30 days.

Chen, H. T. (1934) *Lingnan Sci. J.*, **13**, 75.
—— (1936) *Chin. med. J.*, Suppl. No. 1, 368.
To, Sômei, and Ko, Bun (1935) *J. med. Ass. Formosa*, **34**, 369.
Wang, Shao-Hsun, and Hsieh, C. K. (1937) *Chin. med. J.*, **52**, 829.

PARALYSIS AGITANS

1211 See Surveys and Abstracts 1939, p. 458.

PARAPSORIASIS

DIFFERENTIAL DIAGNOSIS

1213 Much attention has been given to cases of parapsoriasis developing mycosis fungoides tumours, and the general trend of opinion in Great Britain and in America is to regard them as mycosis fungoides in spite of the frequent absence of itching and failure to respond to X-ray therapy.

PARATHYROID GLAND DISEASES

See Surveys and Abstracts 1939, p. 459. **1214-1216**

PAROTID GLAND DISEASES

See Surveys and Abstracts 1939, p. 461. **1217-1226**

PELLAGRA

See also Surveys and Abstracts 1939, pp. 149 and 461.

MORBID ANATOMY AND PATHOLOGY

1228

Nervous system.—Examination of the central nervous system by the Nissl method shows chromatolytic changes of varying degrees of intensity in many nerve cells. The anterior-horn cells of the spinal cord and cells of the cranial motor nerves show this change to a marked degree. In the motor cortex a large proportion of the nerve cells show chromatolysis, the Betz cells being particularly affected. The cells of the frontal and occipital cortex, the hippocampal formations, and substantia nigra show this to a much less degree. The alteration in the spinal cord shown by the Marchi-Busch method is a degeneration of the nerve fibres as a whole. This is usually associated with severe chromatolytic changes in the cell body. The distribution of the lesions in the cord consists of symmetrical degeneration of the dorsal column, especially the column of Goll, and the spino-cerebellar and pyramidal tracts. These cord changes do not resemble those found in subacute combined degeneration.

Treatment

Nicotinic acid continues to give encouraging results in the treatment of pellagra.

Greenfield, J. G., and MacDonald Holmes (1939) *Brit. med. J.*, 1, 815.

PEMPHIGUS AND PEMPHIGOIDS

See Surveys and Abstracts 1939, p. 463. **1229-1233**

PENIS AND SCROTUM DISEASES

See Surveys and Abstracts 1939, pp. 150 and 465. **1234, 1235**

PEPTIC ULCER

See Surveys and Abstracts 1939, pp. 46 and 466. **1236, 1237**

PERITONITIS: III.—TUBERCULOUS PERITONITIS IN CHILDREN

AETIOLOGY

1243

Stubenbord and Spies analysed 257 cases of tuberculous peritonitis obtained from the records of a number of hospitals in New York and Boston; in 118 instances (46 per cent) the patient was under 10 years of age, and the number of cases decreased in each decade up to 70 to 80 (one case). In most series the original tuberculous site is in the intestines, lungs, lymph nodes, or Fallopian tubes, but in the present examination for the presence of tuberculosis in other sites the highest incidence was in the lungs (49 cases); in 142 cases examination of other sites was negative.

Stubenbord, J. G., and Spies, J. (1938) *Surg. Gynec. Obstet.*, **67**, 269.

PHARYNX DISEASES

See Surveys and Abstracts 1939, p. 90. **1245-1257**

PINEAL BODY, TUMOURS

See Surveys and Abstracts 1939, p. 474. **1260**

PINK DISEASE

1261 See Surveys and Abstracts 1939, p. 475.

PITUITARY GLAND DISEASES

1263-1268 See Surveys and Abstracts 1939, p. 476.

PLAGUE

1276 See Surveys and Abstracts 1939, pp. 148 and 479.

PLEURISY

MORBID ANATOMY

1277 The method introduced by Dudgeon and Wrigley of examining fresh films of sputum for the presence of malignant cells can be applied to the examination of pleural fluid. The method is described in the supplementary notes to the article LUNG DISEASES VIII TUMOURS, see p. 127.

Dudgeon, L. S. and Wrigley, C. H. (1935) *J. Laryng.*, **50**, 752

PNEUMONIA, LOBAR

See also Surveys and Abstracts 1939, p. 479

TREATMENT

Non-Specific Treatment

1279 The treatment of pneumonia by the chemo-therapeutic substance sulphanilylaminopyridine (M & B 693) has proved to be of great importance and a real advance. A brief reference to this substance, which had only recently been investigated in the laboratory by Whitby (1938, a) and in the wards by Evans and Gaisford, was made in Vol. IX, p. 737. This substance has since been very extensively used in Great Britain and also in America, where it is employed under the name of sulphapyridine. It has also been used in South Africa, Kenya, India, and the Scandinavian countries with success. It promises to be of as great value in the treatment of pneumonia due to the pneumococcus as the allied substances of the sulphonamide group have proved in streptococcal infections.

It is supplied in tablets each of 0·5 gram. It has a faintly bitter taste and is very insoluble. The tablets may be swallowed whole or given in suspension in water or milk. To produce the best effects relatively high doses are recommended when the drug is first given, followed by a regular 4-hourly dose of smaller amounts when the patient is awake, the object being to achieve a high concentration of the drug in the blood-stream rapidly and to maintain it. The usual dosage recommended in patients severely ill is 2 grams (4 tablets) as an initial dose, followed by a similar amount after 4 hours, and then 1 gram (2 tablets) 4-hourly for about 36 hours, except when the patient is asleep. Usually clinical improvement and a normal temperature result, when the dose may be reduced by giving 1 tablet 4-hourly for another 24 to 36 hours, and then 1 tablet 3 times daily up to a total dose of 20 to 23 grams in a week. Whitby (1938, b) stated that by this means a concentration in the blood of 8 mg. per 100 c.cm. is obtained in 12 hours and maintained at this level throughout the treatment. Evans and Gaisford found that the drug was of no value in staphylococcal, streptococcal, or tuberculous pneumonias. All the drug is excreted within 48 hours after its administration has ceased. Children stand the drug well, and usually with less toxic symptoms than occur in adults. In a child from 6 months to 2 years a dose of 0·25 gram 4-hourly is recommended. It is important that those in charge of the patient should be strictly instructed to avoid the administration of any food containing sulphur, such as eggs, and also sulphates in any form, as these may lead to sulphaemoglobinaemia and cyanosis.

A soluble sodium salt of M & B 693 sold under the name of dagenan-sodium is now available, each ampoule contains the equivalent of 1 gram of M & B 693 in 3 c.cm. of solvent. American authorities claim that this should only be given by intravenous injection considerably diluted owing to its alkalinity. It has been used

intramuscularly by Gaisford (1939) apparently with success, but caution is evidently necessary.

The mode of action of the drug has been studied by Whitby and by Fleming (1938). According to Fleming it retards the growth of pneumococci in human blood in concentrations such as are obtained therapeutically.

Certain toxic effects are observed, notably gastric discomfort and vomiting. These are believed to be due to a local effect and not to any central action. They can be to some extent lessened by powdering the tablets and suspending the powder in hot or cold milk, also by giving alkalis and other gastric sedatives, but vomiting is sometimes a troublesome symptom. It is said by some that nausea may be lessened or avoided by giving smaller doses at hourly intervals. Headache, general malaise, lassitude, and depression also occur, and sometimes a rash, which may be urticarial. Occasionally, in patients receiving large doses, cyanosis and methaemoglobinaemia occur and may necessitate the use of oxygen.

The administration of M & B 693 does not contra-indicate the use of homologous immune serum, which may be given if the case is severe or if the drug fails. Fleming (1939) suggested that probably in the future a combination of treatment by the drug with vaccine therapy might be a valuable routine procedure.

The drug seems valuable also in the treatment of pneumococcal bacteriaemia and in other forms of pneumococcal infections or complications, such as pneumococcal meningitis. It seems to be specially useful in older patients in whom the prognosis has previously been regarded as grave. Gaisford (1939) found that the mortality in patients under 50 was reduced from 16·5 per cent to 1·6 per cent, and in patients over 50 from 51 per cent to 24·4 per cent.

Evans, G. M., and Gaisford, W. F. (1938) *Lancet*, 2, 14
Fleming, A. (1938) *Lancet*, 2, 74
(1939) *Brit. med. J.*, 2, 99
Gaisford, W. F. (1939) *Proc. R. Soc. Med.*, 32, 1070
Whitby, L. E. H. (1938, a) *Lancet*, 1, 1210
(1938, b) *ibid.*, 2, 1015
(1939) *Proc. R. Soc. Med.*, 32, 1063

PNEUMOTHORAX, SPONTANEOUS

See also Surveys and Abstracts 1939, p. 484

TREATMENT

Of High-Pressure Type with Non-Healing Valvular Slit in Lung

1280

Chandler recommended for these cases the following simple method of treatment used successfully in one patient. An artificial pneumothorax refill needle of wide bore, or a small cannula, is inserted into the pleural cavity, to the proximal end of the needle is tied a thin rubber finger-cot, the closed end of which is slit. This makes a perfect valve, allowing air to escape from the pleural cavity but not to return. If the diameter of the needle or cannula is sufficiently large, any amount of air will be blown off from the pleural cavity, and the patient is at once relieved. In the case in point, a man of 58, the heart returned from the mid-axillary line to its normal position in a few minutes, and the cyanosis and dyspnoea were proportionately relieved.

Owing to cough, movements, or surgical emphysema of the chest wall, the needle or cannula is apt to be displaced very soon, the distal end gradually or suddenly working its way into the chest wall, and the valve ceasing to act. To prevent this, Chandler employed the self-retaining cannula recently described by Cope, and tied the finger cot to the curved exit tube. This acted perfectly, the instrument remaining in position for 11 days without displacement. Clotted serum blocked the lumen occasionally, but this was easily dealt with by removing the inner cannula. The most meticulous aseptic and antiseptic precautions must be taken.

There are many objections to using a self-retaining rubber catheter, namely, collapsibility, difficulty of cleaning if blocked, and difficulty with removal and re-insertion. The Cope self-retaining metal cannula obviates such difficulties. It might, however, be possible to use a self-retaining rubber catheter with a cannula, the latter being retained permanently in position. The catheter and cannula, however, would have to be very small, and it is doubtful if the flange of so small a catheter would be sufficiently strong to be really self-retaining.

1280 This valve mechanism, in addition to relieving cyanosis, dyspnoea, and mediastinal displacement, promotes to a great extent re-expansion of the lung. It may succeed in closing the rent, by bringing the ruptured part of the lung up to the chest wall, where adhesions may form. This, however, may not happen, and then, the moment the valve mechanism is removed, the symptoms will recur.

Recourse must therefore be had to injection of gomenol in olive oil, as described in Vol. IX, p. 750. If this fails to irritate the pleura, sodium morrhuate solution might be tried. The rationale of this is to set up a mild aseptic pleurisy with exudation of a small amount of highly fibrinous fluid. This clots and stimulates the process of progressive obliterative pleurisy.

Cope, Z. (1939) *Brit. med. J.*, **1**, 331.

Vol. X POISONS LEGISLATION: MEDICAL ASPECTS

POISONS

Legislation

Poisons List (Amendment) Order, 1939

1281 By this Order benzedrine and sulphanilamide are added to Part I of the Poisons List together with related substances, so that they may be supplied to members of the public only through chemists. Benzedrine is added to the Seventh Schedule and must be labelled 'Caution. It is dangerous to take this preparation except under medical supervision', instead of 'Poison', when made up ready for the internal treatment of human ailments. Benzedrine in inhalers is exempt from all control. Under sulphanilamide and its derivatives the following substances, among others, are included: colsulanyde; P.A.B.S.; prontosil album, streptocide; sulphonamide-P; prontosil soluble; prontosil rubrum, proseptasine (M & B 125); rubiazol; and soluseptasine.

All these substances are added to the First Schedule of the Poisons Rules, and in addition sulphanilamide and its derivatives are added to the Fourth Schedule, and therefore may be supplied only upon the prescription of a duly qualified medical practitioner, registered dentist, or registered veterinary surgeon.

The Poisons (Amendment) Rules, 1938

These rules render it unnecessary for a signed order for a First Schedule poison (other than a 'dangerous drug') from a duly qualified medical practitioner, registered dentist, or registered veterinary surgeon or hospital to bear the statement of the purpose for which the poison is required.

They provide also that local anaesthetics for injection in the treatment of human and animal ailments need not be supplied in fluted bottles.

POLIOMYELITIS AND POLIOENCEPHALITIS

1282 See Surveys and Abstracts 1939, pp. 42 and 484

POST-MORTEM EXAMINATIONS

See also Surveys and Abstracts 1939, p. 487

INFANTICIDE

1287 The Infanticide Bill has now become the Infanticide Act, 1938. It repeals and modifies the provisions of the Infanticide Act, 1922.

PREGNANCY: NORMAL AND PATHOLOGICAL

See also Surveys and Abstracts 1939, pp. 29 and 488.

HAEMORRHAGES

Unavoidable Haemorrhage from Placenta Praevia

Treatment

1295 Browne now considers that the use of the Willett forceps (as described in Vol. X, p. 81) is inadvisable in placenta praevia, as infection with *Cl. welchii* has followed its use

in 2 cases, in one of which the mother died. In using the forceps a wound was made on the foetal scalp, and the compression of the placenta by the continuous weight-traction was apt to kill the foetus; conditions then are ideal for infection by *Cl. welchii*, namely, a lacerated wound in dead tissue. Absence of *Cl. welchii* from the vagina and skin of the perineal region could never be assured, as the organism was very widely disseminated in maternity hospitals. 1295

PREMATURITY

See Surveys and Abstracts 1939, p. 493. 1304

PROSTATE DISEASES

See Surveys and Abstracts 1939, p. 493. 1308

PRURITIS AND PRURIGO (HEBRA)

See Surveys and Abstracts 1939, p. 496 1309, 1310

PSITTACOSIS

See Surveys and Abstracts 1939, p. 496 1311

PSORIASIS

See also Surveys and Abstracts 1939, p. 496.

TREATMENT

Cignolin prescribed in the following paste simplifies local treatment and shortens the course of treatment in many cases of psoriasis. The paste is applied exactly to the patches of psoriasis, being replaced as necessary and not being cleaned off until sufficient reaction has been provoked to clear the psoriasis. The reaction appears very rapidly, often in 3 or 4 days, with this method of application: 1312

Cignolin	–	2 grains
Salicylic acid	–	10 grains
Zinc oxide	}	of each 120 grains
Starch	}	
Soft paraffin	–	to 1 ounce

The addition of H.E.B. Simplex (Halden's Emulsifying Base) in the proportion of 120 grains to one ounce to this paste, or to any pastes or ointments, greatly facilitates their removal by washing and is particularly useful in ointments used on the scalp

PSYCHIATRY OF CHILDREN

See Surveys and Abstracts 1939, p. 497. 1313

PSYCHONEUROSES AND PSYCHOTHERAPY

See Surveys and Abstracts 1939, p. 497. 1315-1317

PSYCHOSES: I.—AFFECTIVE PSYCHOSES

See Surveys and Abstracts 1939, p. 498. 1319

PSYCHOSES: III.—SCHIZOPHRENIA

See Surveys and Abstracts 1939, p. 499. 1321

PSYCHOSES: IV.—TOXIC INFECTIVE PSYCHOSES

See Surveys and Abstracts 1939, p. 505. 1322

PSYCHOSES: V.—ALCOHOLIC PSYCHOSES

1323 See Surveys and Abstracts 1939, p. 505.

PSYCHOSES: VI.—PRE-SENILE AND SENILE PSYCHOSES

1324 See Surveys and Abstracts 1939, p. 506.

PUERPERIUM

See also Surveys and Abstracts 1939, pp. 31 and 507.

PHYSIOLOGY OF THE PUERPERIUM

Superinvolution

1326 If treatment by ovarian hormones is indicated, the new synthetic oestrogen stilboestrol may be administered orally.

MANAGEMENT OF THE NORMAL PUERPERIUM

Posture

1327 Post-natal exercises are of use in promoting involution and general convalescence (Wilson).

COMPLICATIONS OTHER THAN SEPSIS

Bladder Complications

Retention of Urine

1328 In the treatment of retention, injection of mecholyl or doryl may be of value as a preliminary, or alternative, to catheterization

PUERPERAL SEPSIS

Bacteriology

The Infecting Organisms

Puerperal infections due to haemolytic streptococci of group B and the differences between them and infections by group A streptococci have been reported by Fry

Source of the Infecting Organisms

Despite the attention given in recent years to the problems of puerperal infection, the part played by immediate and thorough investigation of early cases in the prevention of an outbreak is not yet fully appreciated. Delay in investigation makes it possible for the infection to be conveyed from patient to patient, and also allows of the possibility of the continued injection of patients by a member of the staff. Since haemolytic streptococci are widely found, and often without any clinical manifestation, it is impracticable to exclude all possible sources of infection from the lying-in woman. But sufficient is known of the importance of the identification of the type of haemolytic streptococci from the cervix of a patient with that obtained from the throat or nose of an attendant, and also of the lines along which an epidemiological study may suitably be carried out, for a procedure in investigation to be established which conforms with present knowledge of the origin and course of outbreaks of puerperal infection and which avoids needless administrative difficulties.

This subject was dealt with in some detail in the Report on an Investigation into Maternal Mortality, 1937 (pp. 239-243), the procedure recommended there for domiciliary and institutional inquiries, based on the practical experience of the medical officers of the Ministry of Health, might suitably be adopted by those responsible for the investigation of outbreaks of infection. Emphasis was laid on the examination of cervical swabs, on serological typing of the organisms found in patients and in attendants, and on the association of bacteriological investigation with clinical examination in the identification of dangerous carriers. The officer responsible for the general investigation should study in detail the obstetric technique adopted and the administration of the institution when in-patients are concerned. It is still too often found that outbreaks of puerperal infection are associated with technique which falls short of the best modern practice and with errors of organization among which overcrowding and over-use of wards still occupy a regrettably prominent place.

On 30th March 1938, the Chief Medical Officer of the Ministry of Health addressed a circular letter to medical officers of health which revises that of 13th April 1934.

In it they are reminded that, on the occurrence of pyrexia in a lying-in woman, appropriate measures should be taken for the isolation of the patient, and that steps should at once be taken to ascertain the cause of the pyrexia. When this is found to be due or suspected to be due to uterine infection, swabs should be taken from the cervix, throat, and nose of the patient. Simultaneously search should be made for any possible source of the infection in persons who conducted the labour or were otherwise in contact with the patient during the subsequent 48 hours. Swabs from the nose and throat and from any obviously infected site should be taken from all contacts. The assistance of the Ministry is available, as formerly, when this help is desired in the investigation of outbreaks.

More recently it is understood that cervical swabbing is being replaced by vaginal swabbing, which is found to be adequate and preferable.

Transference of Infection to Genital Tract

Dust

Cruickshank and Godber investigated the method of spread of streptococcal infections, including 2 small outbreaks of puerperal sepsis, and collected evidence of the importance of aerial spread and of dust-borne infections. In some cases of puerperal sepsis examination of all contacts for carriers is negative, and in such cases the authors believe that an infected atmosphere or infected dust is the source of the infection. In one of their investigations exposure of a blood-agar plate in a ward, from which an infected patient had been removed 6 days previously, provided haemolytic streptococci of the same type as that recovered from the patients in this epidemic. To prevent the spread of organisms by this means, free ventilation of wards, damp sweeping and dusting, and a liberal use of soap and water are effective; sterilization of the air and dust by spraying with aerosols or by ultra-violet irradiation is more expensive, and probably no more effective.

Treatment

Specific Chemotherapy

The report of the Medical Research Council on the use of sulphanilamide is referred to on p. 136. In the place of sulphanilamide, the more recently introduced compound 2-sulphanilylaminopyridine, or M & B 693, is now often used. Experience has shown that it is better to give the sulphonamide compounds (sulphanilamide and M & B 693) in smaller doses more frequently, dividing the total daily amount into 4 or 6 doses. In view of the increased knowledge regarding the toxicity of these drugs, it is now considered that, except in the more severe cases, the dose should not exceed 4 grams daily.

The dangerous toxic effects which may follow the administration of sulphanilamide must be emphasized, as reports of the occurrence of agranulocytosis are increasing in frequency. The experience gained in the prevention and treatment of this complication at Queen Charlotte's Hospital has been summarized by Colebrook, who points out the risk of overlooking the condition because of its insidious onset, and also the high mortality, more than 50 per cent in the recorded cases. Most of the cases of agranulocytosis have followed treatment with sulphanilamide, 6 have been recorded after M & B 693, and one after prontosil-rubrum. In all except 2 cases 30 grams at least of the drug had been given, as the dose necessary to control a severe streptococcal infection is between 20 and 30 grams, the margin of safety is very small. Colebrook considers that, if a patient does not improve during the first 5 or 6 days of treatment, the causal organism is probably not sensitive to the drug. During these first 6 days, if the patient is improving and the fever subsiding, leucocyte counts are not necessary, but, if the temperature does not fall or if there are any disturbing symptoms, such as headache, white-cell counts should be made every second or third day. Whenever more than 25 grams are administered, or the treatment prolonged for more than 10 days, leucocyte counts should be made at short intervals.

In the treatment of agranulocytosis, intramuscular injection of 0·35 gram of pentnucleotide twice daily, and blood transfusion (using defibrinated rather than citrated blood) are useful. A leucocytosis may be induced in the donor by the intramuscular injection of 2 c.cm. of nucleic acid (veterinary nuclein) 4 or 5 hours previous to the collection of the blood.

Colebrook, L. (1939) *Lancet*, **2**, 158.
Cruickshank, R., and Godber, G. E. (1939) *Lancet*, **1**, 741.

1328 Fry, R. M. (1938) *Lancet*, I, 199.
Wilson, J. St. G. (1937) ***Pre-natal and Post-natal Management***, London.

PYELITIS

See also Surveys and Abstracts 1939, p. 508.

TREATMENT

Cure

Subacute and Chronic Pyelitis

1330 The use of sulphonamide drugs has greatly extended (see below).

PYELITIS OF PREGNANCY

Treatment

1331 Sulphanilamide, the drug of the moment in urinary antiseptics, continues to hold an important place in the treatment of pyelitis of pregnancy. Sulphanilamide is more quickly effective than any other standard treatment in pyelitis of pregnancy; a dosage of 0·5 gram 3 times daily rapidly produces a remission of symptoms and in simple cases the urine becomes sterile in from 4 to 5 days. In toxic and severe cases of pyelitis larger doses and more prolonged treatment are necessary to sterilize the urine. Further, the treatment of patients with pyelitis of pregnancy by sulphanilamide is associated with fewer complications than is any other treatment; e.g. premature onset of labour is rare, and the children born are often of normal weight, in contradistinction to the frequency of onset of premature labour (about 30 per cent) and the high still-birth rate and neonatal mortality from underweight and feebleness of the infants.

Speert has shown that sulphanilamide passes readily through the placenta and within 4 hours is present in equal concentration in foetal and maternal bloods. The question naturally arises whether or not the infant suffers; in none of Speert's 40 cases in which large doses of sulphanilamide were used was any such untoward effect noticed in the baby. In view, however, of the known toxic effects of sulphanilamide it is advisable to use the minimal effective dose to cure the pyelitis of pregnancy, to ensure that the concentration of the drug in the foetal tissues is as low as possible.

Speert, H., quoted by Eastman, N. J. (1938) *Int. Clin.*, N.S.I, Vol. 3, p. 303.

PYLORIC OBSTRUCTION

1334-1336 See Surveys and Abstracts 1939, p. 509.

PYOMYOSITIS, TROPICAL

TREATMENT

1337 Sulphonamide compounds, especially uleron, in 3-gram doses for courses lasting 10 to 14 days are indicated.

PYREXIA OF OBSCURE ORIGIN

1338 See Surveys and Abstracts 1939, p. 510.

RADIOLOGY IN DIAGNOSIS AND TREATMENT

1340-1343 See Surveys and Abstracts 1939, p. 511.

RAYNAUD'S PHENOMENON

See also Surveys and Abstracts 1939, p. 518.

AETIOLOGY

Sex Incidence

1345 Adson laid stress on the point that with greater precision and experience in diagnosis, the diagnosis of Raynaud's disease in males was progressively decreasing.

Lewis (1938, a) examined histologically the structure of the arteries supplying the fingers in normal persons and in those with signs and symptoms of Raynaud's disease during life. In hereditary cold fingers the condition of the arteries did not differ from that of normal controls. In Raynaud's disease and sclerodactyly there was intimal hyperplasia, and in the patients with unhealed necrosis of the finger tips the arteries were obstructed by organized thrombi. Lewis also tested the capillary pulsation in these same subjects and concluded that this test gave a reliable indication of the patency of the lumina of the digital arteries: failure to elicit capillary pulsation by immersing the hand in water at 46° C. for 10 minutes indicated considerable reduction or obliteration of the lumen 1345

Treatment

Lewis (1938, b) examined 6 cases of Raynaud's disease after preganglionic sympathectomy, which did not exert any more curative influence than cervico-thoracic ganglionectomy on Raynaud's disease. Clinical improvement followed when the vessels were freed from their normal vasomotor tone, but the local fault in the vessels remained untouched and after operation attacks could still be produced by adequate cooling.

Simmons and Sheehan's investigation of the cause of relapse after sympathectomy performed for Raynaud's disease did not support the hypothesis of Lewis ('local fault') or that of White (sensitization to adrenaline), these authors considered that relapses after preganglionic section and cervico-thoracic ganglionectomy were due to regeneration of sympathetic fibres.

Adson, A. W. (1937) *Surg. Clin. N. Amer.*, **17**, 1051.
Lewis, T. (1938, a) *Clin. Sci.*, **3**, 287.
—— (1938, b) *ibid.*, **3**, 321.
Simmons, H. T., and Sheehan, D. (1937) *Lancet*, **2**, 788

RECTUM DISEASES

See also Surveys and Abstracts 1939, p. 519.

PROLAPSE

Treatment

Surgical

As an additional treatment which may be considered in some cases, the operation of sigmoidopexy may occasionally seem to be indicated, and Pemberton and Stalker have recently described a modification of the old operation of sigmoidopexy. Their method is to incise the peritoneum on each side of the recto-sigmoid, and then to pass the fingers down in the cellular planes as far as the coccyx. The rectum is thus stripped up and pulled up until it is taut, and is then fixed in this new position by sutures. They claim that this operation promises to give good results in advanced cases of complete prolapse. 1347

CARCINOMA

Treatment

Surgical

Excellent results following radical excision of the rectum in A cases of carcinoma (by Dukes' classification) have recently been obtained by Grinnell 1355

Grinnell, R. S. (1939) *Ann. Surg.*, **109**, 500.
Pemberton, J. de J., and Stalker, L. K. (1939) *Ann. Surg.*, **109**, 799

REFLEXES IN DIAGNOSIS

See Surveys and Abstracts 1939, p. 520. 1357

REFRACTION, PRACTICAL METHODS

See also Surveys and Abstracts 1939, p. 521.

Retinoscopy

A self-contained luminous electric retinoscope is now available—the Purvis streak retinoscope. This instrument is particularly valuable for estimating the refraction in bedridden people. The beam of light, or 'streak', is well defined, and can easily 1358

KEY NUMBERS

1358 be rotated by means of a simple device. With this new retinoscope the axis of astigmatism can be accurately located more easily than with other types of instrument.

REJUVENATION

ENDOCRINE TREATMENT OF PREMATURE SENILITY

1360 *Male hormone.* The dosage of testosterone propionate stated at the foot of Vol. X, p. 582, should be 10 to 25 mg. twice weekly by intramuscular injection.

RELAPSING FEVERS

LOUSE RELAPSING FEVER OR EPIDEMIC RELAPSING FEVER

Bacteriology, Morbid Anatomy, and Pathology

1361 Chung and Feng have studied the possibility that the bed-bug may be a vector but conclude that it is unlikely to play any appreciable part in conveying the disease.

Brussin and Sternberg have brought forward experimental evidence that the reticulo-endothelial system plays the chief part in producing antibodies against the spirochaete and that salvarsan acts by directly destroying the spirochaetes. The killed spirochaetes appear to act as vaccines and to give rise to immunity similar to that produced by an untreated attack.

Ts'un and Chung find that a fleeting positive Wassermann reaction occurs during the febrile stage of the disease in about 8 per cent of non-syphilitic patients, other workers have reported a larger percentage of positive reactions but these did not persist after recovery.

TICK RELAPSING FEVER OR NON-EPIDEMIC RELAPSING FEVER

Bacteriology

1362 Recent work tends to confirm the view that this disease is primarily an epizootic of lower animals and that it differs in its clinical manifestations from louse-borne or epidemic relapsing fever.

L'Abbate and Mammino describe a case in which infection was conveyed accidentally to a person by contact of a few drops of heavily infected human blood with an inflamed nasal mucosa. The symptoms were characteristic of tick-borne relapsing fever but the spirochaetes were said to be different from those found in the original patient and to resemble the metacyclic forms described by Leishman in *O. moubata*.

Anderson and Sicart found that infection was conveyed by *Xenopsylla cheopis* from infected rats to other rats kept in an adjoining cage. In this case it seems probable that the transmission was of the direct mechanical type.

Joyeux and Sautet caused infection in rats by feeding them on the brains and viscera of infected rats. The resultant fever was much less severe than that conveyed by infected ticks, it therefore does not seem likely that alimentary infection plays an important part in maintaining the disease among animals.

L'Abbate, G., and Mammino, S. (1938) *Arch. ital. Sci. med. colon.*, **19**, 486.
Anderson, C., and Sicart, M. (1937) *Arch. Inst. Pasteur Tunis*, **26**, 250.
Brussin, A. M., and Sternberg, E. J. (1938) *G. Batt. Immun.*, **21**, 46 and 207.
Chung, H. L., and Feng, L. C. (1938) *Chin. med. J., Suppl.*, no. 2, 563.
Joyeux, C., and Sautet, J. (1938) *Bull. Soc. Path. exot.*, **31**, 279.
Sautet, J. (1937) *Marseille méd.*, **74**, 273.
Ts'un, L., and Chung, H. L. (1938) *Chin. med. J., Suppl.*, no. 2, 315.

RESUSCITATION

See also Surveys and Abstracts 1939, p. 521.

METHODS OF RESUSCITATION

General

Artificial Respiration

1363 *Jacket respirator.* When perfected the device known as the jacket respirator (Burstall) may prove to be as efficient as the cabinet respirators, and seems to be more convenient in use.

Both Respirator

The Both respirators, being distributed by Lord Nuffield's benefaction, work on the same principle as the Drinker but are simpler in construction. 1363

Cardiac Resuscitation

Compounds related to adrenaline.—The properties of the various substitute β-phenylethylamines and β-phenylisopropylamines are gradually being investigated. Gunn gave a summary of the present position in the 1939 Oliver-Sharpey lectures. Apart from the well-known members of the group (adrenaline, ephedrine, benzedrine), several have been used as 'analeptics', notably veritol [β-(*p*-oxyphenyl)-*iso*-phenylmethylamine], which seems to have been used with good results in post-operative and post-anaesthetic shock.

Specific

In Narcotic Poisoning

The value of picrotoxin as an antidote to the barbiturates is described on page 165.

The investigations of Whitehead and Draper confirm the opinion that coramine is of only limited value. They found that it was antidotal against the lighter levels of avertin or ether narcosis, but ineffective against barbiturates. They found evidence that large doses might intensify respiratory depression, that the only local effect on the heart was harmful, and that, in experimental chloroform overdosage, the administration of this drug almost doubled the mortality.

Burstall, A. F. (1938) *Brit. med. J.*, **2**, 611.
Gunn, J. A. (1939) *Brit. med. J.*, **2**, 156 and 214.
Whitehead, R. W., and Draper, W. B. (1939) *Surg. Gynec. Obstet.*, **68**, 892.

RETINA DISEASES

See also Surveys and Abstracts 1939, pp. 130 and 522.

DIAGNOSIS

Vital Staining of the Retina

Sorsby and his co-workers have, for a considerable time, been experimenting with vital staining of the retina with a view to its use in the diagnosis and assessment of disease of the fundus, especially of the retina. 1364

VASCULAR DISEASES

Venous Thrombosis

J. F. Jorpes has recently reported that, out of 20 cases of thrombosis of the central vein of the retina, about 10 recovered with normal or good vision after the administration of heparin. 1367

DETACHMENT

Treatment

Surgical

For the cure of detached retina, there is now more tendency to use indirect ophthalmoscopy with an extremely high candle-power illumination in tracking and localizing the retinal hole. Bipolar surface diathermy is being replaced in many centres by unipolar methods, the amperage being approximately doubled. Probably less stress is now laid on extensive drainage of the subretinal fluid and less reliance is placed on the value of the post-operation position in regard to the drainage of subretinal fluid. 1379

Jorpes, J. F. (1939) *Heparin, its Chemistry, Physiology and Application in Medicine*, London, p. 78.
Sorsby, A., Section 'Vital Staining of the Retina', *Modern Trends in Ophthalmology* (Sorsby, A., and Ridley, F.), London. In press.

RHEUMATIC INFECTION, ACUTE

See Surveys and Abstracts 1939, pp. 135 and 525. 1380

RHINOSPORIDIOSIS

1382 See Surveys and Abstracts 1939, p. 524.

RICKETS

1383, 1384 See Surveys and Abstracts 1939, pp. 38 and 524.

Vol. XI

SCARLET FEVER

See also Surveys and Abstracts 1939, pp. 77 and 525.

TREATMENT

Specific

1387 *Sulphanilamide* - Sulphanilamide has been employed in scarlet fever on the grounds chiefly that the organisms responsible for the disease comprise certain strains of the haemolytic streptococci. Early reports, supported by meagre clinical observations, to the effect that sulphanilamide was effective in controlling the disease have been to a considerable extent discounted by later work. It now appears that sulphanilamide therapy does not influence the toxic stage of scarlet fever, that it has not reduced the incidence of complications, and that it is of no value in reducing the carrier state of discharged patients. Its value as a prophylactic in non-immune contacts is still unsettled. Unless further evidence becomes available to the contrary, it must be concluded that sulphanilamide is of little value in scarlet fever.

Griswold, R. A. (1939) *Ann. Surg.*, **109**, 135.

SCIATICA

1389 See Surveys and Abstracts 1939, p. 526

SCLERODERMIA

See also Surveys and Abstracts 1939, p. 527.

CLINICAL TYPES

Diffuse Scleroderma

With Sclerodactyly

1390 Dowling has discussed 2 cases, with biopsy reports, of diffuse scleroderma with sclerodactyly and myositis, one in a man aged 40 and the other in a woman aged 60. These and other reported cases supported his view that dermato-myositis and symmetrical scleroderma with sclerodactyly were related diseases, and that dermato-myositis was really symmetrical scleroderma with myositis, or myopathy. Damage to muscles was very commonly associated with symmetrical scleroderma with sclerodactyly, and in the biopsies of his 2 cases studied histologically, in one the right triceps and in the other the right thigh muscle, both showed degenerative changes in the muscle.

Dowling, G. B. (1939) *Brit. J. Derm.*, **51**, 82

SCURVY

1391 See Surveys and Abstracts 1939, p. 528

SENESCENCE AND SENILITY

1394 See Surveys and Abstracts 1939, p. 528.

SEPTICAEMIA AND BACTERIAEMIA

See also Surveys and Abstracts 1939, p. 530.

METHODS OF BLOOD CULTURE

1395 Hoare's recent experiments indicate that the routine use of 'liquoid' as an anti-bactericidal substance in blood-culture media should not be recommended, as it

was found to be definitely unfavourable to the growth of anaerobic streptococci, which are commonly present in the blood in puerperal fever and less commonly in other conditions. Sterile trypsin had no such inhibitory effect. 1395

STREPTOCOCCAL BACTERIAEMIA AND SEPTICAEMIA

Loewenthal experimented with mice infected with *Streptococcus pyogenes* Group A, in the hope of reducing the dose of sulphanilamide necessary to protect them by administering simultaneously antistreptococcal serum. This line of attack was suggested by the fact that, as drugs of this group are not bactericidal but only bacteriostatic, the co-operation of phagocytes is required in order to rid the blood of the bacteria. Mouse-protection tests and therapeutic trials both indicated that these 2 therapeutic agents acted in a different but complementary manner, and that the protective effect of either serum or sulphanilamide was enhanced if used in conjunction with the other agent.

Hoare, E. D. (1939) *J. Path. Bact.*, **48**, 573.
Loewenthal, H. (1939) *Lancet*, **1**, 197.

SEX HORMONES

See also Surveys and Abstracts 1939, pp. 17, 34, 108, and 531

USE OF SEX HORMONES IN TREATMENT OF MENSTRUAL AND CLIMACTERIC DISORDERS

Preparations and Standardization of Female Sex Hormones and Gonadotrophic Hormones

The Third International Conference on the Standardization of Hormones was held at Geneva in August 1938. It was agreed that it was both desirable and practicable to establish international standards for the gonadotrophic substance of urine of pregnancy, the thyrotrophic substance of the anterior lobe of the pituitary gland, the lactogenic (crop-gland-stimulating) substance of the anterior lobe of the pituitary gland ('prolactin', 'galactin', 'mammotrophin'), and the gonadotrophic substance of the serum of the pregnant mare. Arrangements were made for the preparation of standards of these substances and for the definition of the units in each case. No decision was reached as to the choice between the suffixes 'tropic' and 'trophic' in the descriptive terms describing the hormones, but in their report the Committee adopt the use of 'trophic' 1397

CLINICAL USE OF MALE SEX HORMONE

Preparations of Male Sex Hormone

The administration of testosterone by mouth was mentioned in Vol. XI, p. 108, recently a derivative ('methyl testosterone') has been found to have greater effect by this route. It is suggested that the methyl group protects the active hydroxyl group from the destructive effects of the fermentative processes in the alimentary canal. Foss has shown that this new product is about twice as potent when tried on an eunuch, whereas in cases of hypogonadism it is effective and rapid in action, and in every way preferable to injection. At present, only the price of this preparation can prohibit its generalized replacement of injection of testosterone propionate when androgen therapy is indicated 1398

Therapeutic Use

Hypogonadism is one of the most important indications for androgen therapy. Cases of adiposo-genital dystrophy and simple hypogonadism are best treated at the time of puberty and show rapid development of the penis and secondary sexual characters. It is wise to combine thyroid therapy and so adjust the whole normal bodily form.

Oral therapy with methyl testosterone is adequate for cases at puberty and small doses only are required – such as 2·5 mg., 4 times daily, for about 6 months. The oral route may prove to be adequate also for older patients, but sometimes injections of testosterone propionate, 50 to 100 mg. daily, may be necessary for adults with genital hypoplasia.

Testicular development is achieved by combined treatment with prolan or pregnyl or other makes of chorionic gonadotrophin.

1398 Testosterone propionate can be used for treating climacteric conditions, but the dose required is high, 30 to 50 mg. per week (Kurzrok, Birnberg and Livingston), and relapses occur on withdrawal. Probably it is best indicated for the poly-oestrin phase, but oestrogens must be preferable and are effective in smaller dosage for the anoestrin phase, and for flushes of the climacteric.

Ill Effects

Doses of 3,000 to 5,000 mg. of testosterone propionate given over a period of months will cause undesirable side-effects in most women, namely an acneiform eruption on the face and body, growth of hair on face and body, deepening of the voice, and enlargement of the clitoris. Of these effects all except the enlargement of the clitoris may be temporary, although it may take some months after treatment has ceased for the voice to return to normal, or for excess hair to disappear. Androgen therapy for women should therefore be used with extreme caution as the effective dose is very near the toxic dose and such treatment is best given by those experienced in its use.

Foss, G. L. (1939) *Brit. med. J.*, **2**, 11.
Kurzrok, L., Birnberg, C. H., and Livingston, S. (1939) *Endocrinology*, **24**, 347.
Report of the Third International Conference on the Standardization of Hormones held at Geneva in August, 1938. (*Quart. Bull. Hlth Org. League N.* (1938) **7**, 889), abstracted in *Endocrinology* (1939), **25**, 318.

SHOCK AND COLLAPSE

See also Surveys and Abstracts 1939, p. 537.

AETIOLOGY

1400 There have been no convincing new investigations on the aetiology of shock. The question of the influence of nerve impulses in causing shock has been the subject of investigations with opposing conclusions. Slome and O'Shaughnessy conclude that nerve-impulses play an important part, whereas Blalock and Cressman, as the result of rather similar experiments, conclude that they are not of leading significance, the chief factor in the production of shock after trauma being fluid-loss in the traumatized area.

HYPOTHESES OF SHOCK

Toxaemia

Allen supports the 'toxaemic' theory. He produced shock in rats by ligature of limbs, when the ligatures were removed after 3 or more hours, or less if more than one limb had been ligatured, marked shock developed, with increased concentration of the circulating blood, reduction of its volume, and migration of fluid to the tissues. Amputation of the asphyxiated limb before release of the ligature, or shortly afterwards, prevented the onset of shock, an observation explicable on the 'toxaemic' hypothesis; moreover, refrigeration of the asphyxiated limbs during the asphyxia inhibited the subsequent shock, whereas warming augmented it. These observations suggested that the toxic substance was a product of the disordered metabolism during the asphyxial period.

TREATMENT

Therapeutically, he found that, after shock was fully developed, the only effective measure was blood transfusion, but the effect of this was transient, and it did not seem to prevent an ultimate fatal outcome. If started before shock was present, saline infusions were the most effective therapeutic measure, blood being less effective at this stage, separated plasma less effective still, and separated corpuscles and acacia solutions completely ineffective. These observations seem to be in harmony with clinical experiences in the human subject.

On the ground that the clinical and biochemical changes in shock resemble those of adrenal cortical insufficiency, as exemplified in Addison's disease, it has been suggested that cortical extract might be useful in the treatment of shock. This has

been tried with promising but as yet inconclusive results in the 'toxaemic' shock following burns (Wilson *et al.*). For other recent therapeutic measures see p. 156. 1400

Allen, F. M. (1939) *Arch. Surg., Chicago*, **38**, 155.
Blalock, A., and Cressman, R. D. (1939) *Surg. Gynec. Obstet.*, **68**, 278.
O'Shaughnessy, L., and Slome, D. (1935) *Brit. J. Surg.*, **22**, 589.
Slome, D., and O'Shaughnessy, L. (1938) *Brit. J. Surg.*, **22**, 900.
Wilson, W. C., Macgregor, A. R., and Stewart, C. P. (1938) *Brit. J. Surg.*, **25**, 826.
— Rowley, G. D., and Gray, N. A. (1936) *Lancet*, **1**, 1400.

SILICOSIS

See Surveys and Abstracts 1939, p. 537. 1401

SKIN DISEASES: II.—OCCUPATIONAL DISEASES

DEFINITION

Table II, Vol. XI, p. 163. The figures for 1937 are as follows 1405

	A	B	A	B	A	B	A	B
1937	784	2650	3	19	74	60	1	25

SKIN DISEASES: III.—LOCALLY INOCULATED INFECTIONS

Streptococcus

Chronic Streptococcal Ulceration

Chronic streptococcal ulceration with the formation of daughter abscesses burrowing into the subcutaneous tissue have been further investigated by Meleney, who claimed that the causal organism was a micro anaerobic haemophilic streptococcus. If this organism is grown anaerobically, after 2 days it will grow aerobically. It then shows the 'alpha' type of haemolysis. Meleney treated the ulceration by laying open all the pockets in the wound and then carefully packing with zinc peroxide cream (zinc peroxide gives off oxygen slowly for 24 hours). 1410

Treatment of recurrences of ulceration

According to Clarkson (personal communication) extensions of ulceration, with tenderness just beyond the edge of the wound, redness, and swelling, associated with a slight rise of temperature, have responded to treatment with sulphanilamide, 4 grams a day for 2 days. The subcutaneous tissue inflammation was re-absorbed without the formation of an abscess breaking down and becoming confluent with the ulcerated area.

SKIN DISEASES: IV.—TUBERCULOSIS

See Surveys and Abstracts 1939, p. 538. 1411

SKIN DISEASES: V.—TUMOURS

See also Surveys and Abstracts 1939, p. 539.

INNOCENT TUMOURS

Derived from Sweat-Glands

Fox-Fordyce Disease

Szép has noticed the occurrence of symptoms due to endocrine imbalance in patients with Fox-Fordyce disease and ascribed this condition to dysfunction of one of the glands, probably the ovaries. He treated a patient with follicular hormone and X-ray irradiation, and in 3 months from the beginning of treatment the condition was greatly improved. 1412

Derived from Bones, and Calcinosis

Calcinosis

1412 Atkinson and Parkes Weber reviewed the subject of cutaneous and subcutaneous calcinosis, grouping cases in which the deposits are confined to special areas as calcinosis circumscripta, and the more serious and often fatal type in which the distribution of the lesions is very variable as calcinosis universalis. They did not include cases of calcinosis in which the skin and subcutaneous tissues are not involved. They recorded the results of blood examination in 20 cases of calcinosis circumscripta and 16 of calcinosis universalis. These did not show any particular abnormality in the haemoglobin or red cells, the leucocytes ranged from 14,500 to 3,900 with polymorphonuclears 76 to 19 per cent (circumscripta), and 23,600 to 4,250, with polymorphonuclears 90 to 44 per cent (universalis); eosinophilia was sometimes present in both forms. The constituents of the blood and metabolic studies were reported in detail, the deposits chiefly contained calcium phosphate and calcium carbonate. The highest blood calcium recorded was 28 mg. per 100 c.cm. (circumscripta). The association of scleroderma with calcinosis circumscripta (40 per cent of 137 cases), and to a less extent with calcinosis universalis (32 per cent of 78 cases) was noted. Raynaud's disease and other vasomotor disturbances were also often associated.

MALIGNANT TUMOURS

Derived from Superficial Layers of Epithelium

Intra-Epidermal Carcinoma

1413 *Paget's disease of the skin.* Weiner has discussed the histogenesis of Paget's 'eczema' and the 57 reported extramammary cases. He concluded that the disease is due to intra-epidermal metastases from a carcinoma of the apocrine sweat glands.

Stout has reported a case of intra-epidermal melanoma (melanocarcinoma) without pigment and closely resembling Paget's disease, and has discussed 6 similar cases previously reported. The site of the tumour is of diagnostic importance, for in the mammary, axillary or genital zones, where Paget's disease may occur, it may be very difficult to distinguish the 2 conditions, whereas in other sites a diagnosis of melanoma is more probable.

Melanotic Carcinoma

Corsi reported the clinical course of three cases of *melanose circonscrite précancereuse* and the results of histological examinations made by Klaber, 2 in women, aged 76 and 87, and one in a man aged 47. The cases were watched through 2, 5, and 12 years. Nodules appeared from time to time and in 2 of the cases were treated by radon seeds. Histologically they differed widely and were difficult to interpret. In the melanotic areas without tumour formation in one case Pagetoid cells were present. The clinical course was more benign than the histology suggested.

SYSTEMIC CONDITIONS

Malignant

Hodgkin's Disease

1415 A case of ulcerative Hodgkin's disease of the skin in a girl, aged 15, was reported by Pessin and Pohle, the twenty-ninth reported case since 1906. It was thought that an osteomyelitic process in the sternum preceded the skin lesions. An abscess developing in the manubrium was curetted twice; 6 months after the first curettage a granulomatous mass had developed at the site of the wound, and the adjacent skin contained elevated white, pinkish, and livid red nodules, and a small lymph node was palpable in the left supraclavicular region and another in the left axilla. Five months later there was a large ulcer over the sternum, and biopsy of a lymph gland revealed typical Hodgkin's disease. Under X-ray therapy the ulcer healed; the patient survived for at least a year (until November 1937) but died after some months (interval not stated).

Atkinson, F. R. B., and Weber, F. P. (1938) *Brit. J. Derm.*, **50**, 267.
Corsi, H. (1939) *Brit. J. Derm.*, **51**, 86.
Dowling, G. B. (1939) *Brit. J. Derm.*, **51**, 82.
Pessin, S. B., and Pohle, F. A. (1938) *Amer. J. Cancer*, **34**, 220.
Stout, A. P. (1938) *Amer. J. Cancer*, **33**, 196.
Szép, F. (1938) *Arch. Derm. Syph., Wien*, **77**, 124.
Weiner, H. A. (1937) *Amer. J. Cancer*, **31**, 373.

SMALLPOX

TREATMENT

Symptomatic

McCammon reported the results of treatment of 7 cases of smallpox. 3 were treated symptomatically and all had typical rashes. 4 were given sulphanilamide in doses of 5 to 10 gr. every 3 hours; 3 of these had only an evanescent macular eruption and one had only 3 pustules. A similar abortive attack following the use of prontosil rubrum was reported by King and De Rozario. **1416**

McCammon, W. O. (1939) *J. Amer. med. Ass.*, **112**, 1936.
King, C., and De Rozario, K. A. (1938) *J. R. Army med. Cps.*, **71**, 404.

SPEECH DEFECTS

See Surveys and Abstracts 1939, p. 542. **1417-1424**

SPINAL CORD DISEASES

See Surveys and Abstracts 1939, pp. 120 and 543. **1425-1433**

SPINE, DISEASE AND DEFORMITIES

See Surveys and Abstracts 1939, p. 544. **1434-1445**

SPLEEN DISEASES

See Surveys and Abstracts 1939, p. 546. **1446-1452**

STERILITY

See also Survey and Abstracts 1939, pp. 157 and 548.

STERILITY IN THE MALE

Diagnostic Testicular Biopsy

In the more obscure cases of male sterility or sub-fertility, when other methods have failed to provide a diagnosis, great help can be obtained from carrying out a testicular biopsy. This can generally be done under local anaesthesia, and without risk to the testicle. All that is necessary is to puncture the tunica albuginea after exposure of the testicle. The small button of testicular tissue that extrudes is cut off with a pair of iridectomy scissors and examined microscopically. This method provides accurate information about the state of the tubules, and is invaluable **1457**

STERILIZATION

See also Surveys and Abstracts 1939, pp. 158 and 549.

STERILIZATION OF THE MALE

Incision.—Vol. XI, p. 474, paragraph 3: for the third and fourth sentences (lines 4 to 8) substitute the following: **1460**

This structure is then carefully separated by dissection from the other constituents of the cord, and two clamps are applied to it at least one inch apart. The intervening portion of the vas is then excised, and the divided ends held by the clamps are ligatured with silk.

STOMACH, TUMOURS AND SOME OTHER CONDITIONS

See Surveys and Abstracts 1939, p. 549. **1461-1464**

STRABISMUS

1465 See Surveys and Abstracts 1939, p. 551.

SYMPATHETIC AND PARASYMPATHETIC NERVOUS SYSTEM

1466 See Surveys and Abstracts 1939, p. 552.

SYPHILIS

See also Surveys and Abstracts 1939, pp. 151 and 553.

TREATMENT

Pyretotherapy

1467 A report by Krusen and Elkins on fever therapy by physical means, authorized by the Council on Physical Therapy of the American Medical Association, indicates that in early primary syphilis, a combination of artificial fever therapy and chemotherapy gives better results than either treatment alone. By inducing a body temperature of above 105° F. (40.5° C.) during 10 sessions each of 5 hours, and combining a course of 30 injections of an antisyphilitic drug, cutaneous lesions react promptly and may be free from living spirochaetes after the first fever session. The serological reactions also improve under this treatment

Krusen, F. H., and Elkins, F. C. (1939) *J. Amer. med. Ass.*, **112**, 1689.

TALIPES

1468, 1469 See Surveys and Abstracts 1939, p. 558

TAPEWORM INFECTIONS, INTESTINAL

1470-1473 See Surveys and Abstracts 1939, p. 558

TESTIS AND CORD DISEASES

1475-1479 See Surveys and Abstracts 1939, p. 559.

TESTIS, UNDESCENDED

See also Surveys and Abstracts 1939, p. 561

TREATMENT

1480 *Testosterone propionate.* Testosterone propionate has been increasingly employed of late in the treatment of hypogonadism due to cryptorchidism and the consensus of opinion is that it constitutes an effective substitution therapy. Kearns, for example, investigated its use in castrates and in cryptorchids. The usual dosage he employed was 10 mg. twice weekly, but in 2 out of 6 cases 5 mg. twice weekly was sufficient to produce and maintain increased strength and endurance, and a desire to expand their work. There also appeared libido, erections, ejaculations, ability for coitus, and an increase in the growth of the beard. After 3 to 6 weeks the prostate was found to have regenerated perceptibly and in from 6 to 8 months it approached its normal size. The author also found that testosterone in the form of an ointment (2 mg. of testosterone in each c.cm.) gave excellent results, at least equal to those obtained with injections. A total average weekly dose administered to castrates was 20 mg. by injection and 28 mg. by inunction. Patients were directed to rub in the ointment vigorously for 20 minutes at bedtime into a hairless region of the skin, preferably on the anterior abdomen.

Kearns, W. M. (1939) *J. Amer. med. Ass.*, **112**, 2255.

Vol. XII

TETANUS

1481 See Surveys and Abstracts 1939, p. 562.

TOXICOLOGY: I.—HOMICIDAL, SUICIDAL, AND ACCIDENTAL POISONING

See also Surveys and Abstracts 1939, p. 565.

SYNTHETIC ORGANIC SUBSTANCES

Cyclic Ureides and Barbituric Acid

1496

Treatment.—As a result of favourable results obtained in animal tests, picrotoxin has been tried clinically in barbiturate poisoning. Before using this drug it is important to make a certain diagnosis of the cause of the patient's condition as there is definite evidence that the drug is dangerous in cases of morphine poisoning.

The dose of picrotoxin is 0·5 to 2 mg. and there is a very narrow margin of safety In barbiturate poisoning, however, much higher doses can be used. The drug must be given in divided doses of 3 to 10 mg Overdosage must be avoided, since a convulsive attack is followed by increased depression. In most of the reported cases the drug had been given intravenously during the first stages of the treatment, at intervals of 20 minutes to an hour until the patient responded. Since picrotoxin is detoxicated fairly rapidly in the body, to be effective the amount present in the blood must be maintained. As the patient improves the intramuscular route may be employed.

Experimental tests reported by Bleckwenn *et al* (1937) showed that 1 mg. of picrotoxin was an antidote for 30 to 40 mg. of pentobarbital sodium, sodium amytal, or their thio derivatives. Bleckwenn and Masten later (1938) reported on the use of picrotoxin in 6 patients poisoned with barbiturates taken with suicidal intent. They recommend for an emergency treatment administration of picrotoxin intravenously in a 1 in 1,000 solution at a rate of 1 c.cm. per minute until pupillary and corneal reflexes return, and subsequently subcutaneous administration. The total amount administered to each of 5 patients who recovered varied from 24 mg. to 148 mg.; 669 mg. were administered to one patient who died, and it was considered this was probably more than was necessary.

The dose of barbiturate which had been taken was not always known, and the recovery of some of the drug by gastric lavage reduced the amount absorbed, the time that had elapsed since taking the drug was also a factor causing variation in the amount of antidote required. The cases reported by Bleckwenn and Masten received the following dosage (i) 24 mg. picrotoxin, patient confessed to having taken 8 capsules each of 3 gr. of sodium amytal. (ii) 669 mg. picrotoxin; it was estimated that the patient had taken 75 gr. of sodium amytal and 18 gr. of pentobarbital sodium; patient died. (iii) 68 mg. picrotoxin. (iv) 148 mg. picrotoxin, patient had taken 156 gr. of sodium amytal (v) 60 mg. picrotoxin, patient had taken 80 gr. of sodium amytal and 6 gr. of phenobarbital (vi) 30 mg. picrotoxin; patient had taken 120 gr. of sodium amytal As additional measures to counteract the narcosis, they recommended gastric lavage, and purgation (magnesium sulphate not recommended), continuous oxygen, promotion of diuresis by parenteral fluids and intravenous sucrose, and the oral administration of dextrose to prevent acidosis.

Bleckwenn, W. J., and Masten, M. G. (1938) *J. Amer. med. Ass.*, 111, 504.

— — and Tatum, A. L. (1937) *J. Pharmacol.*, 60, 99

TOXICOLOGY: II.—INDUSTRIAL POISONING

See also Surveys and Abstracts 1939, p. 570.

NITRO- AND AMINO-DERIVATIVES

Tetryl

1536

Leigh-Silver, of the Royal Arsenal, Woolwich, writing on the diseases which occur in filling factories, describes poisoning by tetryl Tetryl (trinitrophenylmethylnitramine) causes yellow staining of the hands of workers in 1 to 3 days and of the face and scalp in 1 to 3 weeks; sunlight deepens the colour It does not cause constitutional symptoms but, unless precautions are taken, is a potent source of dermatitis, though susceptibility varies greatly. Tetryl irritation may release an attack of chronic skin disease. The rash generally affects the face first, especially

1536 the sides of the nose, and around the eyes and the corner of the mouth; it is intensely irritable. Later the condition spreads to the chin, neck, and back of the head, and may lead to a papular eruption. There are no characteristic changes in the blood.

Prophylaxis

Protective clothing should be provided. Shops should be well ventilated, and the atmosphere dry. Great care should be taken to avoid raising dust. The hands should be washed thoroughly in running water before the face is washed. The addition of 5 per cent sodium sulphite will assist removal of tetryl by converting it into a soluble substance. Workers should be warned against the use of proprietary ointments. A water-soluble skin varnish should be used on the face and arms before beginning work. Susceptible persons should be removed from contact with the substance; convalescents are particularly susceptible.

Treatment

Oils and ointments aggravate the condition, but a soothing lotion, such as calamine lotion, should be applied. After the acute inflammation has subsided the affected parts may be cleansed with olive oil. Workers who recover from an acute attack in less than a fortnight may be allowed to resume contact work after a further week. Legally these cases are entitled to compensation for the period of disability.

Leigh-Silver, A. L. (1938) *J. R. Army med. Cps.*, **71**, 87

TRACHEA DISEASES

1541-1544 See Surveys and Abstracts 1939, p. 573.

TRACHOMA

1545 See also Surveys and Abstracts 1939, p. 573.

Errata. In Vol. XII, p. 218, last paragraph, 1st line, and p. 219, top line, for 'lid' read 'lip' as follows: p. 218 'The lower lip' . . ., and p. 219 'The wound in the lip' . . .

TREATMENT

Conclusion

Sulphanilamide. P. Richards *et al.* employed sulphanilamide in 12 Indian children all of whom showed trachoma with follicular atrophy and pannus. Striking improvement occurred in all cases, and after 4½ months the conjunctivae in each case had become smooth and free from follicles. Corneal infiltrates disappeared in all eyes except one, and the corneal activity was apparently checked. In 2 untreated children, used as controls, there was no apparent improvement during the period of observation, but improvement rapidly occurred when sulphanilamide was given later. Sulphanilamide therapy effected the disappearance of the epithelial-cell inclusion bodies characteristic of active trachoma.

Richards, P., Forster, W. G., and Thygeson, P. (1939) *Arch. Ophthal., N.Y.*, **21**, 577

TRENCH FEVER

1548 See Surveys and Abstracts 1939, p. 574.

TRICHINIASIS

See also Surveys and Abstracts 1939, p. 575.

CLINICAL PICTURE

1549 Evers reported the case of a man, aged 25, admitted to hospital in coma with a history of a rash consisting of small red spots surrounded by larger red blotches; these disappeared after the application of a simple soothing lotion. Neuro-retinitis was present, and the cerebrospinal fluid contained motile trichinella larvae. The blood showed 38 per cent of eosinophils. Recovery took place.

Of 24 collected cases with the larvae in the cerebrospinal fluid, 4 proved fatal; but the presence of larvae in the cerebrospinal fluid was not always accompanied by clinical symptoms. In 15 cases there were signs of encephalitis, such as delirium, stupor, or coma, and often loss of the deep reflexes. In 8 cases meningitis had occurred. **1549**

Evers, L. B. (1939) *Arch. intern. Med.*, **63**, 949.

TROPICAL DISEASES, GENERAL SURVEY

See Surveys and Abstracts 1939, p. 576. **1550, 1551**

TRYPANOSOMIASIS

See Surveys and Abstracts 1939, p. 576 **1553**

TUBERCULOSIS

See Surveys and Abstracts 1939, p. 577 **1554**

TUBERCULOSIS, GENERALIZED

See Surveys and Abstracts 1939, p. 582. **1555**

TULARAEMIA

See Surveys and Abstracts 1939, p. 582 **1556**

TUMOURS

See Surveys and Abstracts 1939, p. 583. **1557**

TYPHUS FEVERS

See Surveys and Abstracts 1939, p. 583 **1558-1560**

UNDULANT FEVER (*MELITENSIS* AND *SUIS* TYPES)

See Surveys and Abstracts 1939, p. 584. **1571**

URETHRA DISEASES

See Surveys and Abstracts 1939, p. 584 **1573, 1574**

URINE EXAMINATION

See Surveys and Abstracts 1939, p. 585 **1575**

UROGENITAL ORGANS, ABNORMALITIES

See Surveys and Abstracts 1939, p. 586. **1576-1578**

UTERUS, DISEASES AND DISORDERS: I.—DEVELOPMENTAL ABNORMALITIES

See Surveys and Abstracts 1939, p. 587 **1580**

UTERUS, DISEASES AND DISORDERS: IV.—TUMOURS

See Surveys and Abstracts 1939, p. 588. **1586-1590**

UVEAL TRACT DISEASES

1591-1594 See Surveys and Abstracts 1939, p. 590.

VACCINIA AND VACCINATION

1595 See Surveys and Abstracts 1939, p. 590.

VEIN DISEASES

1596 See Surveys and Abstracts 1939, p. 591.

VERTIGO

1598 See Surveys and Abstracts 1939, p. 593.

VITAMINS

See also Surveys and Abstracts 1939, p. 594.

WATER-SOLUBLE VITAMINS

Vitamin B_1 and Beri-Beri

Symptoms of Overdosage

1602 Steinberg has reported that, among over 300 patients treated with large doses of various preparations of the vitamin B complex or vitamin B_1 for chronic arthritis, herpes zoster occurred in 3 cases and symptoms suggesting spasm of smooth muscle in 2 others. The dosages in the 3 patients developing herpes zoster were as follows: (i) 800 units of vitamin B_1 orally and 2,000 units intravenously at weekly intervals; after 4 weeks typical herpes zoster lesions were present on the arm and chest; (ii) 2,000 international units intravenously at weekly intervals, and 800 units daily by mouth, after 5 weeks herpes zoster developed on the arm and chest; (iii) 1,200 international units of vitamin B_1 daily by mouth; after 2 months herpes zoster developed on the right upper elbow. The lesions in all cases disappeared 3 to 8 weeks after cessation of treatment. One patient after 6 months' massive treatment noticed a sense of fullness in the epigastrium, and a feeling of constriction of the throat within 2 minutes after an intravenous injection. Another felt constriction in the throat and severe cramps after several months of treatment. Steinberg considers that these two cases suggest either the development of sensitivity to vitamin B_1 or supersaturation of the tissues.

FAT-SOLUBLE VITAMINS

Dihydrotachysterol (A.T. 10)

1607 Dihydrotachysterol is a dihydro derivative of tachysterol, which is an isomer of ergosterol produced by irradiation of ergosterol. It is claimed that this substance raises the serum calcium to normal and relieves tetany in hypoparathyroidism. MacBryde found that 6 women suffering from chronic hypoparathyroidism (of 3½ to 17 years' duration), and one with idiopathic tetany, were completely relieved of their symptoms by doses of 0·3 to 1·0 c.cm. daily, supplemented by calcium lactate or gluconate 4 to 10 g. daily.

Hurxthal and Claiborne treated 6 patients with post-operative tetany of at least 2 years' duration with dihydrotachysterol. They found that 2 to 5 c.cm. weekly controlled the milder cases, but that larger doses were required in more severe cases. It is advisable to give calcium orally in addition, preferably calcium lactate.

Jacobi and Tigges tested the effect of dihydrotachysterol in 8 patients with various disorders. In one with tetany and hypocalcaemia which followed removal of a goitre the symptoms were relieved. In a case of sprue with severe hypocalcaemia the serum calcium was restored to normal with relatively small doses. In a case of idiopathic tetany with normal blood calcium the symptoms were cured. In another patient with idiopathic tetany and hypocalcaemia small doses were effective. On the other hand treatment was unsuccessful in the following: a patient with excretory pancreatic insufficiency, colitis, and megacolon together with signs of tetany and hypocalcaemia; a child with nephrosis and hypocalcaemia without

tetany, and a case of osteitis fibrosa cystica. One woman tolerated unusually large doses for 2 years, but showed no rise in the blood calcium.

OTHER VITAMINS

Vitamin K

1608

Dam of Copenhagen showed in 1935 that deficiency of a fat-soluble substance in the diet of newly-hatched chicks caused a fatal haemorrhagic diathesis associated with a low plasma prothrombin level. The condition could be prevented or cured by administration of a protective factor which Dam called vitamin K.

A substance (or substances) possessing this protective property is present in the green parts of plants such as alfalfa, spinach, kale, tomatoes, chestnut leaves, carrot-tops, and oats. It can also be extracted from putrefied fish meal or rice bran, in which it is probably formed by bacterial action.

Attempts have been made to establish a unit of measurement of vitamin K (Dam's unit, for example, is defined as the amount of antihaemorrhagic material in one g. of dried spinach). Further information concerning the chemical and biological properties of the vitamin is, however, necessary before a satisfactory unit can be established.

The clinical use of vitamin K in the treatment of bleeding associated with obstructive jaundice is described on page 113.

During the past four years much activity has been directed towards the isolation in pure form of vitamin K_1 and its synthesis. In 1933 Almquist prepared a colourless, crystalline, fat-soluble substance which was heat stable, but rapidly destroyed by alkalis or sunlight. This substance had a vitamin K potency 8 times greater than that of ordinary extracts of alfalfa. Work carried out by Klose *et al* indicated that the properties of the vitamin were those of a complex unsaturated hydrocarbon of high molecular weight. Thayer *et al.* also isolated a crystalline compound of high potency from alfalfa leaves. More recently, Dam *et al* prepared, by a process of molecular distillation and chromatographic methods, a constant product which is thought to be pure vitamin K. This is a clear yellowish oil containing carbon, hydrogen, and oxygen, and free from nitrogen. It is said to contain 20,000,000 Dam units per gram. McKee and his associates reported the isolation of vitamin K_1 from alfalfa, and K_2 from putrefied fish meal, and provided evidence which indicated a quinoid structure for these vitamins.

Almquist and Klose have recently reported that phthiocol (2-methyl-3-hydroxy-1:4-naphthoquinone) possesses physical and chemical properties similar to pure vitamin K. Phthiocol was first isolated in 1933 by Anderson and Newman from the pigment of *Mycobacterium tuberculosis*, and it was prepared synthetically in 1934. Almquist and Klose have shown that the antihaemorrhagic property of phthiocol lies between that of methyl naphthoquinone and hydroxy-naphthoquinone. This work indicated that the methyl group is functionally important, whereas the hydroxyl group appears to reduce activity. They concluded that the activity of phthiocol is lower than that of the more complex form of vitamin K in alfalfa. Thayer *et al.* and several workers have recently reported tentative structural formulae for vitamins K_1 and K_2. It appears probable that within a few months pure synthetic vitamin K will be available for clinical use.

Almquist, H. J. (1937) *J. biol. Chem.*, **120**, 635.
— and Klose, A. A. (1939) *J. Amer. chem. Soc.*, **61**, 1611.
— — (1939) *ibid.*, **61**, 1923.
Anderson, R. J., and Newman, M. S. (1933) *J. biol. Chem.*, **101**, 773.
— — (1933) *ibid.*, **103**, 197.
Dam, H. (1935) *Nature, Lond.*, **135**, 652.
Dam, H. G. A., Glavind, J., Karrer, P., Karrer, W., Rothschild, E., and Salomon, H. (1939) *Helvet. chim. Acta*, **22**, 310.
Hurxthal, L. M., and Claiborne, T. S. (1939) *New Engl. J. Med.*, **220**, 911.
Jacobi, J., and Tigges, F. (1939) *Dtsch. Arch. klin. Med.*, **183**, 558.
Klose, A. A., Almquist, H. J., and Mecchi, E. (1938) *J. biol. Chem.*, **125**, 681.
MacBryde, C. M. (1938) *J. Amer. med. Ass.*, **111**, 304.
MacCorquodale, D. W., Binkley, S. B., Thayer, S. A., and Doisy, E. A. (1939) *J. Amer. chem. Soc.*, **61**, 1928.

1608 McKee, R. W., Binkley, S. B., MacCorquodale, D. W., Thayer, S. A., and Doisy, E. A. (1939) *J. Amer. chem. Soc.*, **61**, 1295.
Newman, M. S., Crowder, J. A., and Anderson, R. J. (1934) *J. biol. Chem.*, **105**, 279
Steinberg, C. Le R. (1938) *Amer. J. digest. Dis.*, **5**, 680.
Thayer, S. A., Cheney, L. C., Binkley, S. B., MacCorquodale, D. W., and Doisy, E. A. (1939) *J. Amer. chem. Soc.*, **61**, 1932.
MacCorquodale, D. W., Binkley, S. B., and Doisy, E. A. (1938) *Science*, **88**, 243

VULVA AND VAGINA DISEASES

1610-1612 See Surveys and Abstracts 1939, p. 600.

WHOOPING-COUGH

1613 See Surveys and Abstracts 1939, p. 601.

YAWS

1615 See Surveys and Abstracts 1939, p. 604.

YELLOW FEVER

1616 See Surveys and Abstracts 1939, p. 604.